UNIVERSITY OF ALBERTA

THE EFFECT OF DIABETES STATUS ON SIX MONTH FUNCTIONAL OUTCOME POST JOINT ARTHROPLASTY

BY

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A thesis submitted to the Faculty of Graduate Studies and Research in partial fulfillment of the requirements for the degree of **MASTER OF SCIENCE**

IN

REHABILITATION SCIENCE–PHYSICAL THERAPY

FACULTY OF REHABILITATION MEDICINE

EDMONTON, ALBERTA

Spring 2007

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Ottawa ON K1A 0N4
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Your file Votre référence
ISBN: 978-0-494-29928-9
Our file Notre référence
ISBN: 978-0-494-29928-9

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DEDICATION

This work is dedicated to my loving and supporting wife, Apinke Ubaidat, and my children, Ali, Haneef and Alya.

ABSTRACT

PURPOSE: The purpose of this study was to determine the effect of diabetes on six-month function and change in function (effect size) post joint arthroplasty and to compare functional outcomes of participants with (DM) and without (NDM) diabetes.

METHODS: A secondary analysis was done on the data collected through a primary prospective study of a cohort of 715 participants with elective Total Hip and Knee Arthroplasty (TJA). Function was evaluated pre-operatively and at six-months post-operatively using the Western Ontario and McMaster Universities (WOMAC) Osteoarthritis Index. Independent variables examined included age, gender, education, pre-operative function and pain, Body Mass Index, depression, co-morbidities, joint operated, and post-operative complications.

RESULTS: Participants with diabetes had lower ($p < 0.05$), but clinically insignificant, function at six months. There was no significant association between DM and the six-month function and effect size.

CONCLUSIONS: Diabetes status alone may not be a reason to expect reduced function after TJA.

ACKNOWLEDGEMENT

My appreciation and special thanks go to Dr Sharon Warren for great mentorship and tutelage, support and encouragement. It was an excellent experience completing this project under your supervision.

My gratitude also to my committee members: Dr Allyson Jones, Dr Lauren Beaupre and Dr Scot Simpson. Your inputs were invaluable and contributed to the successful completion of this work. I am highly indebted to the duo of Drs Jones and Beaupre for giving me access to the data used for this study.

My appreciation to staff and colleagues who have supported me in one way or the other: Angela Libutti, Segun, Jian Ghangri (for the use of PASS® for my sample size calculation), and Lori Schaump.

I would also like to thank the following friends: Ismail, Oredegbe, Anthony, Adeyoriju, Muideen, Tayo Ikun, TJ Longus, Sulaiman, Ola and Susan, Nazeef, Awon ti Adinni forever, Dr A. Pedro, and my co-workers at the Two Hills Health Centre.

My very special thank to my parents- thanks all over again. And to Dr Amusat and the rest of the Amusat family back home in Nigeria I say thanks a bunch.

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CHAPTER ONE

INTRODUCTION

1.1 PROBLEM STATEMENT

Arthritis affects people of all ages and ethnic backgrounds, and osteoarthritis, the commonest of the arthritic conditions, affects about 10% of Canadian adults (Health Canada, 2003). Total Joint Arthroplasties (TJA) are the recommended treatment for end stage osteoarthritis (American College of Rheumatology (ACR), 2000). Current utilization rates for Total Hip and Total Knee Arthroplasties (THA and TKA) in Canada have increased by approximately 54% when compared with rates from the 1990s, with similar trends reported in the United States of America (USA) (American Academy of Orthopedic Surgeons (AAOS), 2003; Canadian Joint Replacement Registry (CJRR), 2004). Between 1993 and 2002, utilization rates in the USA increased by approximately 35% for THA and 70% for TKA (Katz, 2006). This increase may reflect age associated higher incidence of degenerative joint disease requiring these types of procedure, technological advancement in surgical techniques, and better outcomes.

Apart from the high level of patient satisfaction (Roder et al., 2003), studies have shown that pain and functional improvement occur after THA and TKA (Bachmeier et al., 2001; Fortin et al., 1999). Greater than 85% patient satisfaction rates have been reported regarding met expectations and outcome (Mancuso, Salvati, Johanson, Peterson, & Charlson, 1997; Roder et al., 2003). The greatest amount of recovery occurs in the first three to six months post-operation (Fitzgerald et al., 2004; Jones, Voaklander, & Suarez-Almazor, 2003), with approximately 50% of pain relief and functional improvement occurring within the first three months following surgery (Bachmeier et al., 2001; Brander et al., 2003).

Despite reports of good outcomes post joint arthroplasty, an estimated 15-30% of patients may still have little or no improvement or may feel unsatisfied with their outcomes (Jones et al., 2003; Jones, Voaklander, Johnston, & Suarez-Almazor, 2000; Nilsdotter, Petersson, Roos, & Lohmander, 2003). While recovery rates may not be the same for all patients, identifying patients who may need intensive post-operative rehabilitation has often been a challenge. Identifying predictors of functional outcomes could guide in knowing patients that may require this additional therapy.

Predictors of functional recovery after arthroplasty have been sparsely studied. It also seems that outcome predictors are many, and knowledge about them is minimal (Jones, Beaupre, Johnston, & Suarez-Almazor, 2005). Presence of chronic co-morbid conditions is one of the factors that could influence functional outcome (Nilsdotter et al., 2003; Fortin et al., 1999). As the utilization of TJA increases with age so does the prevalence of chronic conditions (Gilmour & Park, 2006). Chronic conditions often impact on multiple dimensions of health including function (Gilmour & Park, 2006; Maddigan, Feeny, & Johnson, 2004). This impact of chronic conditions varies with the specific condition. Diabetes Mellitus (DM) is a chronic condition that is very prevalent in the elderly and influences overall health including function. The influence of diabetes on short-term functional outcomes after TJA has not been widely studied.

Diabetes Mellitus is a multi-system disorder characterized by biochemical and anatomical abnormalities (e.g. the diabetic vascular dysfunction) due to disturbance of glucose homeostasis (England, Stern, Insall, & Windsor, 1990). Diabetes is a common condition worldwide and its prevalence has been rising steadily (Yang, Yeo, Lee, & Lo, 2001). The prevalence of diabetes among American adults aged ≥18 has increased from 4.9% in 1990 to 7.9% in 2001, an increase of 61% (Mokdad et al., 2003). Thus, about 16.7 million Americans had diabetes in 2001. The increase in the prevalence rate of diabetes observed from 1990 to 2001 affected both genders and all socio-demographic groups studied (Mokdad et al., 2003). In 2001, the prevalence rates of diabetes in people aged 50-59, 60-69 and ≥70 years were 11.2%, 15.1% and 15.5% respectively (Mokdad et al., 2003). According to the Canadian Community Health Survey (CCHS) of 2000-2001, the prevalence of diabetes in Canada was 7.24% and 12.96% in people aged 50-64 and 65-74 years respectively (Kelly & Booth, 2004). The data above also illustrate that the prevalence of diabetes increases with age (Health Canada, 2002; Young & Millar, 2003).

The problem of diabetes is a growing one given its association with obesity, which is an increasing public health problem in North America (Harris et al., 1998; Mokdad et al., 2003). Better health screening, public awareness, increased longevity for people with the disease, and lowering of the plasma glucose cut off point to diagnose the disease are among the reasons that have been given for the increased prevalence (Harris et al., 1998; Yang et al., 2001). Despite positive results from better screening methods, many cases of diabetes still go undiagnosed (Health Canada, 2002; Meding et al., 2003). Complications of diabetes manifest in many body organs. It is known to affect skin and bone healing, delay collagen synthesis, and increase infection rate through impaired phagocytic function (Goodson & Hunt, 1977, & 1979; Loder, 1988; Robertson & Polk, 1974).

These effects of diabetes may be more pronounced in the elderly because they are prone to have degenerative joint diseases and other co-morbidities. Effects of diabetes on many body organs may translate into reduced function and mobility after surgery such as joint arthroplasty. Diabetes has been shown to be associated with reduced subjective and objective function (Gregg et al., 2000, & 2002; de Rekeneire et al., 2003; Wu et al., 2003). The independent role of DM in reducing function has been debated (de Rekeneire et al., 2003). Maddigan, Feeny and Johnson (2005) reported a significant reduction in the health utility score in individuals with DM as the number of co-morbid conditions increased. These authors concluded that the burden of illness in DM was related more to the accompanying co-morbid conditions. Accounting for the effect of co-morbidities attenuated DM's association with reduced function in most of the other studies reviewed, but significant association persisted (Gregg et al., 2000; Maty et al., 2004; de Rekeneire et al., 2003). It therefore seems that DM has a unique independent contribution to the functional deficit that has been reported in people with the disease. However, presence of co-morbid conditions may have an additive effect in causing reduced function (Wee, Cheung, Li, Fong & Thumboo, 2005). The independent influence of diabetes on functional outcome after TJA has not been explored.

Previous studies of the effects of diabetes on the results of THA and TKA have focused on long-term clinical and radiological outcomes, and did not control for the influence of existing co-morbid conditions and other factors that could influence function (England et al., 1990; Meding et al., 2003; Moeckel, Huo, Salvati, & Pellicci, 1993; Papagelopoulos, Idusuyi, Wallrichs, & Morrey, 1996; Serna, Mont, Krackow, & Hungerford, 1994; Yang et al., 2001). No study was found in the literature that has reported on the effect of DM on short-term function or change in function after arthroplasty while controlling for relevant demographics, medical and clinical factors that could influence function. The purpose of the study was to evaluate the effect of DM status on short term function while controlling for covariates that could influence function.

1.2 OBJECTIVES

1. The primary objective of this study was to determine whether diabetes status (having diabetes or not) is an independent determinant of functional recovery following TJA after adjusting for other potential patient characteristics that could influence function.
2. The secondary objective was to determine whether the six-month joint specific function as defined by the WOMAC function subscale scores

and effect size of patients with diabetes (DM) differs from those patients without diabetes (NDM) after receiving TJA.

1.3 RESEARCH HYPOTHESES

The following hypotheses were tested:

1. Diabetes will negatively impact the six-month WOMAC function and effect size (post-operative minus pre-operative score divided by the standard deviation of pre-operative score) post TJA after controlling for other covariates which could influence function. These include age, gender, education, pre-operative function, pre-operative pain (WOMAC joint pain and Health Utility Index 3- HUI3- single attribute pain scores), Body Mass Index (BMI), depression, co-morbidities, type of joint operation and post-operative complications.

2a. The six-month post-operative WOMAC physical function scores of DM patients will be significantly higher (clinically) than the pre-operative WOMAC function scores.

2b. The six-month WOMAC function and the WOMAC function effect size will be significantly higher (clinically) after TJA for NDM than patients with DM.

2c. The pre-operative WOMAC function scores of patients with DM will be significantly lower (clinically) than scores for NDM.

1.4 ETHICAL CONSIDERATIONS

Information gained from the results of this study provided an insight into the effect of DM status on functional outcomes after TJA. This study involved the use of anonymous secondary data. All privacy regulations (University of Alberta and Capital Health) relating to the proper use and disposal of secondary data were adhered to. The Health Research Ethics Board of the University of Alberta approved the study.

CHAPTER TWO

LITERATURE REVIEW

2.1 OSTEOARTHRITIS

2.1.1 Definition

The primary reason for undergoing TJA is for relief of symptoms of arthritis. Arthritis and related conditions make up a large group of disorders affecting joints, ligaments, tendons, bones and other components of the musculoskeletal system. Arthritis is the leading cause of pain, physical disability and use of healthcare services in Canada. Osteoarthritis (OA) is the most common of these joint diseases (Health Canada, 2003). Defining OA is complex because it can be a radiological disease only or have both radiological and clinical manifestations. A consensus definition of OA that takes disease complexity into consideration is given as follows: "OA diseases are a result of both mechanical and biologic events that destabilize the normal coupling of degradation and synthesis of articular cartilage chondrocytes and extracellular matrix, and subchondral bone. Although they may be initiated by multiple factors, including genetic, developmental, metabolic, and traumatic, OA diseases involve all of the tissues of the diarthrodial joint. Ultimately, OA diseases are manifested by morphologic, biochemical, molecular, and biomechanical changes of both cells and matrix which lead to a softening, fibrillation, ulceration, loss of articular cartilage, sclerosis and eburnation of subchondral bone, osteophytes, and subchondral cysts. When clinically evident, OA diseases are characterized by joint pain, tenderness, limitation of movement, crepitus, occasional effusion, and variable degrees of inflammation without systemic effects" (Sherma, Kapoor & Issa, 2006).

Table 2-1: American College of Rheumatology Osteoarthritis Diagnostic Criteria (Altman, 1995)

Hip OA clinical and radiographic diagnostic criteria

(Patient must meet criteria 1, 2, 3 or 1, 2, 4 or 1, 3, 4)

1. Hip pain for most days of the prior month
2. ESR ≤ 20 mm/h (laboratory)
3. Radiograph femoral and/or acetabular osteophytes
4. Radiograph hip joint-space narrowing

Knee OA clinical diagnostic criteria

(Patient must meet criteria criteria 1, 2, 3, 4 or 1, 2, 5 or 1, 4, 5)

1. Knee pain for most days of prior month
2. Crepitus on active joint motion
3. Morning stiffness ≤ 30 minutes in duration
4. Age ≥ 38 years
5. Bony enlargement of the knee on examination

Knee OA clinical and radiographic diagnostic criteria

(Patient must meet criteria criteria 1, 2 or 1, 3, 5, 6 or 1, 4, 5, 6)

1. Knee pain for most days of prior month
2. Osteophytes at joint margins (radiograph)
3. Synovial fluid typical of OA (laboratory)
4. Age ≥ 40 years
5. Morning stiffness ≤ 30 minutes
6. Crepitus on active joint motion

2.1.2 Diagnosis of OA

There are different diagnostic criteria for OA since there is no constant relationship between joint pain and the radiological features of OA. For this reason, prevalence and incidence studies relying on evidence of joint degeneration alone may yield a higher number of affected individuals compared to studies where combination of joint degeneration and joint pain are used for the diagnosis of OA. This is because individuals with evidence of degeneration may not be showing clinical signs of the disease (Arden and Nevitt, 2006). The most widely used diagnostic criteria were developed by the American College of Rheumatology (ACR) (Table 2-1) (Altman, 1995); these criteria emphasize having joint pain for most days of the prior month (Arden and Nevitt, 2006).

2.1.3 Types of OA

Osteoarthritis has been divided into two major types (primary and secondary) depending on whether there is a known cause for the joint degeneration. Primary OA occurs in the absence of a known cause for joint degeneration and is rarely found in people younger than 40 years. Secondary OA, which has obvious causes, may occur in younger adults (Buckwalter, Saltzman, & Brown, 2004). Some of the secondary causes of OA are joint injuries, developmental and hereditary joint diseases, joint infection, neuropathic joints and aseptic joint necrosis. All synovial joints can be affected by OA and the pattern of how they are affected varies. Primary OA is common at the knee and the hip joints (Buckwalter et al., 2004).

2.1.4 Risk Factors of Osteoarthritis

There are many risks factors associated with OA. Previous studies on risk factors have not separated the risk factors for incident disease and those for disease progression until recently (Sherma et al., 2006). There are, of course, some overlap in how these risk factors affect incident disease and its progression. The risk factors for incident disease are genetic factors, congenital and developmental deformities of the joint, aging, injury to the joint, occupational and non-occupational physical activities, obesity, bone mineral density and estrogen deficiency. Risk factors for the progression of the disease are nutritional factors, varus-valgus alignment, meniscus tear and extrusion, hip abduction moment, muscle strength and bone mineral density (Sherma et al., 2006). Some of these factors in various forms have been discussed by other authors (Arden & Nevitt, 2006; Buckwalter et al., 2004; Felson, 2004; Felson, Lawrence, Dieppe, Hirsch, & Helmick, 2000; Jordan et al., 2000; Health Canada, 2003). Out of all the modifiable risk factors, obesity has particular relevance to this study because it both increases the risk for diabetes mellitus and osteoarthritis.

Obesity has been shown to be a risk factor for the development of knee osteoarthritis and for the progression of radiological osteoarthritis (Anderson & Felson, 1988; Felson, Anderson, Naimark, Walker, & Meenan, 1988; Mokdad et al., 2003). Gelber et al. (1999) reported that male medical students who had BMI ≥25 between the ages of 20 and 29 years had a three-fold increased risk of developing symptomatic knee osteoarthritis by the age of 65 years. The risk of developing knee OA was greater for people with weight gain resulting in a shift from normal to overweight within the range of 20-50 years (Manninen, Riihimaki, Heliovaara, & Suomalainen, 2004). Coggon et al. (2001) also reported progressively increased risk of knee OA as BMI increases. Compared to BMI of 24 to 24.9, the risk of OA knee increased from an Odds Ratio (OR) of 0.1 (95% Confidence Interval (CI) 0.0, 0.5) for a BMI < 20 to OR of 13.6 (95% CI 5.1, 36.2) for a BMI of ≥36. If overweight and obese people decreased their weight by 5kg or until BMI was within the recommended range, 24% of surgical cases of knee OA might be avoided (Coggon et al., 2001). Obesity is associated more with knee than hip OA (Gelber et al., 1999).

The mechanism by which obesity influences onset and progression of OA is unclear. Metabolic factors and increased biomechanical load across articular cartilage have been postulated as possible mechanisms (Powell, Teichtahl, Wluka, & Cicuttini, 2005). While a biomechanical component probably mediates large joint OA, it may not be the sole means by which obesity contributes to the pathogenesis of OA given that the disease often exists in non-weight bearing joints (Powell et al., 2005). The fact that OA is often present in non-weight bearing joints of obese compared to thinner women has fuelled speculation about the role of genetics, which until now has not been fully examined. Powell et al. (2005) opined that genetic components may be mediated by altered metabolic factors such as those that result in obesity.

2.1.5 Prevalence and Incidence

Osteoarthritis affects people of all ages and ethnic groups. It is estimated that 10% of people over the age of 60 years suffer from OA worldwide; 80% of these people have limitation of movement and 25% cannot perform major daily activities (Buckwalter et al., 2004). Approximately 40 million (15%) Americans suffered from some form of arthritis in 1995, and greater than 20 million may be suffering from OA (Lawrence et al., 1998). The Canadian Community Health Survey (CCHS) done in the year 2000 showed that arthritis and rheumatic conditions affected nearly four million Canadians aged 15 years and older, which constituted 16% of the total population or approximately one of every six Canadian (Health Canada, 2003). It is projected that approximately six million Canadians will be living with arthritis by the year 2026, an increase of 54% from the current rate (Health Canada, 2003). Osteoarthritis, the most common of the arthritic conditions, affects about 10% of Canadian adults (Health Canada, 2003). The prevalence and incidence of OA increases with age, a trend that will continue as the population ages (Arden & Nevitt, 2006; Buckwalter et al., 2004; Health Canada, 2003). However, OA is not a disease of the elderly alone because in the Canadian Community Health Survey, only two of every five people with arthritis were 65 years or older (Health Canada, 2003).

There is evidence pointing to the presence of gender differences in the prevalence and incidence of OA, with females generally at a higher risk (Srikanth et al., 2005). Maillefert et al. (2003) found that women presented with more severe symptomatic polyarticular osteoarthritis and that structural progression of the disease was more rapid in women than in men. Similarly, Srikanth et al. (2005) reported that females, particularly those equal to or greater than 55 years of age, tended to have severe OA in the knee, but not other sites. In the CCHS survey (2000), women reported higher rates of arthritis compared to men (19% versus 11%, $p < 0.05$) (Health Canada, 2003). Despite the pattern of gender differences for prevalence and incidence of OA, Maillefert et al. (2003) surmised that explaining gender differences is complex because OA in women may be related to other systemic diseases which may have rapid progression for OA.

2.1.6 Burden of OA to the Individual and Society

Once OA has developed, it is a life long disease with periods of exacerbation and remission of its clinical features, which include increasing pain and severity of disability. Therefore, it is readily understandable why OA places significant burden on individuals affected and the society where they live. The burden of OA requires careful consideration of the direct, indirect and intangible costs. Direct and indirect costs represent the total financial burden while intangible costs describe the quality of life related costs on which no fiscal value can be accurately placed (Stafinski & Menon, 2001). There has been no study of the direct costs of OA alone for Canada (Stafinski & Menon, 2001). The costs of all musculoskeletal diseases to Canadians in 1993 were calculated to be $2.46 billion for direct costs and $17.9 for indirect costs (Moore, Mao, Zhang, & Clarke, 1997). In another study reporting on the costs of rheumatism and arthritis in 1994, the estimated figure was $2.12 billion for direct costs, which was 2.9% of the total Canadian health expenditures for that year, and $3.75 billion for indirect costs (Badley & Williams, 1998). An estimated 60 billion in direct costs is spent annually in the USA on OA (Buckwalter et al., 2004).

2.2 TOTAL HIP AND TOTAL KNEE ARTHROPLASTY

The utilization rate for Total Joint Arthroplasty (TJA) has been rising partly because of the success of surgery due to improved technologies and an aging population with increasing life expectancy (CJRR, 2004). In the United States, approximately 170,000 Total Hip Arthroplasy (THA) and 300,000 Total Knee Arthroplasty (TKA) are performed annually (American Academy of Orthopaedic Surgeons (AAOS), 2003). In Canada, statistical data for THA and TKA are summarized in the Canadian Joint Replacement Reports (CJRR), the most recent of which was 2005. A total of 48,419 THA/TKA procedures on Canadian residents were done in 2002/2003, about a 54% increase compared to the 1994-95 data (31,463) and a one year increase of 10.1% from 43,979 done in 2001-2002. The annual rate for TKA has always surpassed that of THA and the gap is increasing. In 2002-2003, there were more TKA procedures (26,500) compared to THA (21,919) (CJRR, 2005). Total Knee Arthroplasty increased by 77.4% compared to 1994-95 (up by 9.6% from the previous year) while THA increased by 32.6% (up by 10.7% from the previous year). However, the number of orthopedic surgeons available for these TJA may not be keeping up with demands. The Canadian national median wait time from referral to treatment for an orthopedic surgeon increased 65%, from 19.5 weeks to 32.2 weeks, between

1993 and 2003. The number of orthopedic surgeons per 100, 000 Canadian population is 3.1 (Comeau, 2004).

There are also provincial variations in the number of THAs and TKAs performed in Canada during the 2002-2003 (CJRR, 2005). The age-standardized rates for THA were highest in Saskatchewan and lowest in Quebec (80.8 and 42.3 per 100, 000 respectively in 2002). The rates for TKA were highest in Manitoba with Quebec having the lowest (97.9 and 43.7 per 100,000 respectively in 2002). Alberta had a total of 1,999 and 2,501 primary THA and TKA respectively in 2002 (23% and 72% increase compared to 1994-95).

The mean age of people having THA and TKA was greater than 65 years in both the USA and Canada (AAOS, 2002 & 2003; CJRR, 2005). In 2002-2003, the mean age for patients who had THAs and TKAs in Canada were respectively 68 and 68.7 years. Sixty-five percent and 69% of these patients were 65 years or older for THA and TKA respectively (CJRR, 2005).

Women were more likely to have both THAs and TKAs compared to men (59% and 41% for THA, 61% and 39% for TKA respectively for females and males). The age-standardized rates of both THA and TKA for women were higher than that of men in 2002-2003 (65.3 per 100,000 and 56.2 for THA, 84.1 per 100,000 and 65.9 for TKA respectively for females and males). Patients having both THA and TKA were rarely underweight (2% and 1% respectively) (CJRR, 2005). Patients having TKA were more likely to be overweight or obese compared to those with THA (87% and 72% respectively) (CJRR, 2005).

Disparities in access to arthroplasty surgery, which are not based on clinical needs but influenced by gender, racial/ethnic, and socioeconomic status have been reported (Hawker et al., 2000; Skinner, Weinstein, Sporer, & Wennberg, 2003). Hawker et al. (2000) reported that despite equal willingness in both genders in their Canadian study, women were less likely to have discussed the possibility of arthroplasty with a physician and equally less likely to undergo arthroplasty. Skinner et al. (2003) reported differences in the annual rates of TKA among Hispanics, blacks and non-Hispanic white men and women in the USA. The rates were higher for non-Hispanic white women than for Hispanic and black women. Similarly, non-Hispanic white men had higher rate than Hispanic men and more than double the rate for black men.

Functional Outcomes after THA and TKA

Total joint arthroplasty has become the standard treatment for end stage osteoarthritis (ACR, 2000). Total joint arthroplasty is very effective with very low mortality (CJRR, 2005; Mahomed et al., 2003). Significant pain relief and improvement in functional status have been achieved after joint arthroplasty (Brady, Masri, Garbuz, & Duncan, 2000; Fortin et al., 1999; Hawker et al., 1998; Mahomed et al., 2002). These gains attributed to TJA extend to patients even at age 80 and above (Jones et al., 2001).

The greatest amount of improvement takes place within the first three to six months after surgery, with long lasting gradual improvements thereafter (Aaron, Hall, Hughes, & Salmon, 1996; Kirwan, Currey, Freeman, Snow, & Young, 1994). Fitzgerald et al. (2004) reported that patients with THA and TKA had markedly reduced physical function around one month post-operation but by three months showed improvement. Patients with TKA recorded initial dramatic functional gains after operation, but subsequently these gains are less than the improvement shown by the patients with THA (Aarons et al., 1996; Bachmeier et al., 2001). This may be crudely reflected in the length of hospital stay (LOS) after these procedures. Patients with THA stay on the average longer than TKA (9.6 days and 7.4 days respectively) (CJRR, 2005). Bachmeier et al. (2001) observed a change of 68% in physical function after THA compared to 43% after TKA. Jones et al. (2001) reported that patients with THA reported 46% improvement in function, while patients with TKA had 34% improvement regardless of age. Fitzgerald et al. (2004) explained that the differences in function may be related to patients with TKA having more pain initially after operation. However, by six months, patients with TKA and THA had similar functional outcomes. Despite reports of very good functional improvement after arthroplasty, patients may not have comparable function to that of the general population matched for age and gender. Patients with TKA matched for age and sex scored significantly lower in function at six months on the SF-36 when compared with the normative data of the general population for the United States (Jones et al., 2003).

Improvement in pain after TJA has been a large part of the reported success with these procedures. Joint pain improves significantly after joint replacements (Brander et al., 2003; Nilsdotter et al., 2003; Jones et al., 2001). Jones et al. (2001) observed that the effect size for pain reduction was more than the effect size for functional gains after THA and TKA. Brander et al. (2003)

reported that significant pain was recorded at all follow-up periods (until 12 months in their study). Fewer patients reported significant pain as time passed by, with about 44.4% and 22.6% reporting significant pain (Visual Analogy Scale > 40) at one and three months respectively. Differences in the level of pain post-operatively may be different between patients with THA and TKA. Jones et al. (2001) reported that patients with THA reported 38% reduction in pain, while patients with TKA had only 28%, regardless of age. Fitzgerald et al. (2004) reported that patients with TKA may have more pain initially after operation; but that by six months, the pain level in patients with both TKA and THA was similar.

Some patients report little or no improvement in physical function and pain after TKA. Jones et al. (2003) reported about 28% improvement in the WOMAC function score overall, but 20% of patients still did not have a 10-unit change in function at six months after TKA. About 60% of the patients with TKA continue to have moderate to extreme difficulty for heavy domestic duties (like vacuuming) and descending stairs. Improvement in function as reported by the Medical Outcomes Study Short Form Health Survey (SF-36) was even less (24%) for patients with TKA (Jones et al., 2003). Lack of improvement may be related to continuing pain (Brander et al., 2003), continuing difficulty with activities (Jones et al., 2003), or inappropriate pre-operative expectations about outcomes (Mahomed et al., 2002). Similarly, for pain, Brander et al. (2003) noted in their study that about 18% and 13% of patients continue to report significant pain six and 12 months respectively after TKA. Nilsdotter et al. (2003) observed that about 22% of the patients after THA did not improve at least 10 points for pain.

Functional Outcome in patients with Diabetes after THA and TKA

Diabetes mellitus is increasing in the general population, with the elderly having the highest prevalence (Health Canada, 2002). It is logical to expect an increasing number of elderly patients with diabetes to have joint arthroplasty because this surgical procedure is common in the older age groups. As utilization begins to increase, there is more focus on outcome after joint arthroplasty especially in patients with other chronic conditions (Meding et al., 2003). Improved functional outcome has been reported post TKA in people with diabetes (Meding et al., 2003; Yang et al., 2001). However, most studies have actually focused on the survivorship of prosthetic implants and clinical outcomes such as rates of complications in these patients (England et al., 1990; Meding et al., 2003; Moeckel et al., 1993; Papagelopoulos et al., 1996; Serna et al., 1994; Yang et al., 2001).

Yang et al. (2001) reported significant improvement in the post-operative functional score on the Knee Society Clinical Scale in a pre- and post-TKA comparison. Meding et al. (2003) matched patients with and without diabetes who received TKA during a similar period and found that functional score post-operatively was significantly lower in patients with diabetes. The authors attributed this result to possible chronic complications of diabetes mellitus

Patient satisfaction after TJA

Most patients receiving TJA are usually satisfied with the outcomes. Satisfaction with outcomes at short to mid-term follow-up after THA was more than 93% in a cohort of 21,997 patients (Roder et al., 2003). Mancuso et al. (1997) also reported a high satisfaction rate of about 89% after THA. The satisfaction levels reported in two studies after TKA were slightly less at just above 80% (Hawker et al., 1998; Robertsson, Dunbar, Pehrsson, Knutson, & Lidgren, 2000).

Patient satisfaction after TJA is strongly associated with overall post-operative outcomes and how well these meet pre-operative expectations (Mancuso et al., 1997). Patients who expect complete pain relief post-operatively have better functional outcomes (Mahomed et al., 2002), which may increase satisfaction level. There is a strong influence of psychology in explaining satisfaction level of patients after TJA. Mancuso et al. (1997) reported that patients expecting psychological benefits (e.g. feel better, remove shame and stigma, enjoy life again, and hope for the best) have more satisfaction (96% versus the overall satisfaction rate of 89%).

Satisfaction is not highly correlated with disease or general health outcome ratings. Robertsson and Dunbar (2001) reported correlations ranging between 0.20 and 0.68 for satisfaction and common TJA outcome tools, with correlations for the WOMAC subscales being between 0.63 and 0.67. Bullens, van Loon, de Waal Malefijt, Laan, and Veth (2001) on the other hand, reported correlations between 0.48 and 0.62 on the Knee Society Rating, VAS pain and

WOMAC tools; the WOMAC items were moderately correlated with satisfaction (0.48 to 0.56). Bullens et al. (2001) concluded that patients and surgeons may be using different criteria in estimating satisfactory outcome after TJA, with surgeons being generally more satisfied.

2.3 DIABETES MELLITUS (DM)

2.3.1 Prevalence of DM

As the utilization of TJA increases with age, so does the prevalence of chronic conditions (Gilmour & Park, 2006). Chronic conditions often impact on multiple dimensions of health, including function (Gilmour & Park, 2006; Maddigan et al., 2004). The impact of chronic conditions varies with the specific condition. Diabetes is one of the chronic conditions that are very prevalent in the elderly, which influences overall health, including function.

Diabetes Mellitus (DM) is one of the leading chronic diseases affecting 8% of our population (Health Canada, 2002), and its prevalence is increasing worldwide (Young & Millar, 2003). More than one million new cases are diagnosed each year, and prevalence has more than tripled since 1970 in the United States' population (Meding et al., 2003). This increased prevalence is attributable to a combination of demographic, lifestyle and clinical factors (Young & Millar, 2003). Despite better screening, it is believed that many cases of DM (up to one-third of cases) remain undiagnosed (Health Canada, 2002; Meding et al., 2003).

Diabetes is reaching an epidemic rate in both men and women and across all socio-demographic groups in both Canada and USA (Health Canada, 2002; Mokdad et al., 2003). In Canada, 4.8% of people aged ≥20 years had DM in 1998-99 (Health Canada, 2002). According to the CCHS survey of 2000-2001, the prevalence of diabetes in Canada was 7.2% and 13.0% in people aged 50-64 and 65-74 years respectively (Kelly & Booth, 2004), and 13.5% in those over 75 years old (Young & Millar, 2003). The prevalence of diabetes increases with age (Health Canada, 2002; Tang & Chen, 2000); Young and Millar (2003) have described it as a disease of the elderly. In addition to an age bias in prevalence, males have been found to have higher rates (4.8% versus 4.2% in females in 2000-2001).

Provincial analysis in Canada showed the highest prevalence of DM in Nova Scotia (5.2%), the lowest in Yukon (3.5%), with Alberta having a prevalence of 3.9% (data were age- and gender-standardized). Cumulative incidence over four years showed that 1.4% of adults developed diabetes during 1998-99 (Health Canada, 2002).

It is worthwhile to note that these epidemiologic data, including the Canadian National Diabetes Surveillance System (CNDSS) data, do not differentiate between types 1 and 2 DM. As the disease characteristics are substantially different, this is a recognized limitation of the current case definitions (Health Canada, 2002).

2.3.2 Types and Diagnosis of DM

Diabetes mellitus (DM) is a chronic condition that results from the body's inability to sufficiently produce and/or properly use insulin (Health Canada, 2002). Insulin is a pancreatic hormone needed to absorb glucose from the bloodstream by the different cells of the body for eventual energy production. Deficiency of insulin production or resistance to insulin activity leads to hyperglycemia, which has been reported to adversely affect many body organs (Einhorn et al., 1988), sometimes, resulting in organ failure in long standing cases. DM can be divided into three main forms: Type 1, 2 and gestational diabetes.

Type 1 diabetes (IDDM) is an autoimmune disease in which the insulin-producing cells of the pancreas produce little or no insulin. It is thought to be due to a combination of genetic factors and environmental stressors (Health Canada, 2002). This type of diabetes occurs in childhood or early adolescence, and treatment entails administration of insulin. Symptoms may include dysuria, dysphagia, dyspepsia, weight loss, blurred vision, and fatigue. Type 1 DM represents about 10% of the total DM population (Health Canada, 2002).

Type 2 diabetes (NIDDM) is the most common form of diabetes, constituting about 90% of the total DM population (Young & Millar, 2003). It typically occurs after the age of 40 years and is found in a higher proportion of overweight individuals. Type 2 DM is considered to be one member in a group of disorders which may include insulin resistance, cholesterol and lipid disorders, obesity, high blood pressure, high risk of blood clotting, and disturbed blood flow to many organs (Centers for Disease Control and Prevention, 1997). Although the mechanisms of Type 2 DM are not fully understood, it may involve the following stages: insulin resistance, postprandial hyperglycemia (when the pancreas is unable to produce enough insulin to overcome resistance), and fasting hyperglycemia (American Diabetes Association, 2000).

Gestational diabetes (GDM) occurs in about 4% of women during pregnancy and ends after birth (Young & Millar, 2003). It is a risk factor for type 2 DM in later life.

Diagnosis of DM based on the criteria in the Canadian Diabetes Association Clinical Practice Guidelines (2003) is given in Table 2-2.

Table 2-2: Diagnosis of Diabetes from the Canadian Diabetes Association Clinical Practice Guidelines (2003)

Fasting Plasma Glucose ≥7.0 mmol/L
Fasting = no caloric intake for at least 8 hours

or

Casual Plasma Glucose ≥11.1 mmol/L + symptoms of diabetes
Casual = any time of the day, without regard to the interval since the last meal
Classic symptoms of diabetes = polyuria, polydipsia and unexplained weight loss

or

2hr Plasma Glucose in a 75-g Oral Glucose Tolerance Test (OGTT) ≥11.1 mmol/L

(A confirmatory laboratory glucose test (an FPG, casual PG, or a 2hrPG in a 75-g OGTT) must be done in all cases on another day in the absence of unequivocal hyperglycemia accompanied by acute metabolic decompensation).

2.3.3 Complications of DM

Individuals with DM experience substantial illness burden due to the disease and associated co-morbid conditions. Microvascular complications of DM include retinopathy, neuropathy, and nephropathy, and the macrovascular complications include cardiovascular disease (coronary artery disease) and cerebro-vascular disease (i.e. stroke). Approximately 60% of individuals with DM have one or more complications (Liebl et al., 2002).

Diabetes is known to affect many body organs, and its effects may reduce function and mobility after surgery such as joint arthroplasty (Meding et al., 2003). Previous studies in patients with DM after joint arthroplasty have documented decreased wound healing, decreased implant survivorship, and increased superficial and deep wound infection (Meding et al., 2003; Papagelopoulous et al., 1996; Yang et al., 2001).

2.3.3.1 Delayed Wound Healing

Normal wound healing is complex and dynamic, and the full mechanisms are still not understood (Christopherson, 2003). A summary of the stages of the normal wound healing process is given in Table 2-3 (Christopherson, 2003; Terranova, 1991). Surgical procedures entail an assault on a patient's body and, as such, can place the body under a great deal of stress (Pearl & Kanat, 1988). Healing time is lengthened in the presence of diabetes (Greenhalgh, 2003), and the impact on cost of care is great, considering the increasing number of people with diabetes who will need care for their wounds. There are many reasons for impaired healing in people with diabetes: impaired circulation, altered metabolic status and collagen synthesis are some that have been discussed in the literature (Lioupis, 2005).

Table 2-3: Stages of normal wound healing

Stage	Time frame	Physiological events
Inflammatory	Injury to about 4-5days	Vascular response- vasoconstriction and platelet aggregation with fibrin to form a clot. Signs of inflammation such as redness, swelling, increased temperature and capillary permeability. Polymorphonuclear leukocytes arrive to combat infection and remove dead tissue.
Proliferative	5th to 20th day	New capillaries form, fibroblasts activated to synthesize collagen and proteoglycans. Adequate oxygen is required for these activities.
Maturational	20th day to 2 years	Collagen tissue remodeling. Wound achieves about 80% of its former strength.

Effect of Impaired Circulation on Wound Healing

(a) Atherosclerosis: This condition is very common in people with diabetes, and it is related to vascular stenosis and reduced blood flow (Greenhalgh, 2003). Reduced blood flow decreases the amount of oxygen available for the healing processes, including collagen formation, and the bacteria-killing oxidative mechanism (Lioupis, 2005). Availability of oxygen is further compromised by the impaired oxygen-unloading of glycosylated hemoglobin (see below for a detailed discussion).

b) Microcirculation (Micro-vascularity): Transportation and exchange of nutrients, waste products of metabolism, tissue defense, and repairs occur at the microcirculation level (Tooke, 1995). It is therefore logical to assume that any defect in microcirculation will affect wound healing. Thickening of the basement membrane has been observed in patients with DM (Flynn & Tooke, 1992). Two mechanisms have been described for the thickening of the basement membrane.

First, in poorly controlled type 1 DM, increased skin capillary pressure occurs, though it readily reverses with good glucose control (Silhi, 1998; Young, Veves, & Boulton, 1993). Increased skin capillary pressure leads to thickening of the basement membrane, which modifies and affects efficient microcirculation (Young et al., 1993). Second, persistent hyperglycemia encourages the conversion of glucose to sorbitol in the endothelial cells. Edema results because sorbitol cannot diffuse across the cell membrane, leading to metabolic and membrane function alteration and basement membrane thickening (Christopherson, 2003).

Hyperglycemia also leads to the production of endothelium derived relaxing factor, which may explain the vasodilatation seen early in DM (Pober & Cotran, 1990). At the inflammatory stage of healing, the effect of the basement membrane thickening and abnormal levels of circulating endothelial factors halt the normal hyperemic response, thereby reducing the normal inflammatory indicators (Christopherson, 2003; Silhi, 1998).

Effect of Altered Metabolic Status on Wound Healing

Hyperglycemia is associated with impaired healing in DM. Prevention of hyperglycemia has resulted in improved wound healing (Goodson & Hunt, 1979). An increased glucose level adversely affects cell function in many ways.

a) First, hyperglycemia leads to the production of Advanced Glycosylation End Products (AGEs). AGEs are aggregates of aldoses covalently bonded to reactive amino acids (Greenhalgh, 2003; Lioupis, 2005). These glycosylated products result in endothelial cell dysfunction and increase the permeability of blood vessels, causing a thickened and inelastic vessel wall, and thus reducing blood flow. AGEs also lead to increased oxidative stress and altered collagen degradation due to cross-linkages. AGEs are chemotactic for monocytes, inducing the production of platelet-derived growth factors leading to changes typical of atherosclerosis (Lioupis, 2005).

b) Second, an elevated glucose level increases Protein Kinase C (PKC) activity. PKC is a key signaling receptor for many cellular activities including proliferation, contraction, calcium influx, hormone receptor turnover, and neovascularization (Greenhalgh, 2003; Lioupis, 2005). Cellular Na/K ATPase activity is also altered by hyperglycemia. This process involves the action of aldose reductase reducing glucose to sorbitol, which can increase osmotic load in the cells (Silhi, 1998).

c) Third, increased blood viscosity caused by altered Red Blood Cells (RBCs) has been attributed to hyperglycemia (Morain & Colen, 1990). Increased viscosity may result in stasis, occlusion, ischemia, and hypoxia. The viscosity may be due to stiffened RBCs, which are likely to aggregate because of their decreased ability to deform and pass through capillaries. RBC membrane stiffness and aggregation seem to be due to non-enzymatic glycosylation of the RBC membrane protein. Glycosylated RBCs have impaired oxygen-unloading because of their affinity for oxygen (Lioupis, 2005; Morain & Colen, 1990). Impaired oxygen unloading may result in tissue hypoxia (Christopherson, 2003).

Effect of Defective Collagen Synthesis on Wound Healing

Collagen synthesis is the hallmark of the second (proliferative) stage of wound healing (Christopherson, 2003; Terranova, 1991), and it relates to both skin and musculoskeletal healing. The accumulation of hydroxyproline, a component of collagen, is reduced in wounds of people with diabetes (Goodson & Hunt, 1977). Insulin has been shown to be essential for fibroblastic activity, especially in Type 1 DM, and early insulin therapy improves collagen synthesis (Goodson & Hunt, 1978). Hyperglycemia results in glycosylation of collagen, resulting in highly inflexible collagen prone to eventual breakdown (Lioupis, 2005). AGEs also mediate covalent cross-linkage of collagen, which alters its degradation. There is also a decreased level of ascorbic acid in patients with DM, which may contribute to unstable and poor collagen structure (Silhi, 1998).

Ascorbic acid (Vitamin C) is considered to be a free radical scavenger that is necessary to prevent oxidative damage.

Bone (musculoskeletal) healing, like skin wound healing, involves similar phases (Kagel & Einhorn, 1996). Insulin directly increases collagen production by osteoblasts (Gabbitas, Pash, & Canalis, 1994). Bone healing is affected at both the primary and secondary levels in DM (Loder, 1988). The primary union is decreased by the reduced activities of the osteoblasts, while at the secondary levels, union is decreased by impaired cellular proliferation, ground substance production, vascular ingrowths, and remodeling (Loder, 1988). Collagen cross-linkage is impaired, making collagen degradation easy for the enzyme collagenase (Einhorn et al., 1988). There is an increase in the appearance time and delayed maturation of chondrocytes in fractured callus (Macey et al., 1989).

Animal studies have shown that the cellular changes could partly be corrected by insulin therapy (Goodson & Hunt, 1977; Macey et al., 1989). Macey et al. (1989) noted that the insulin needed may be in a dose that failed to normalize the blood glucose level (hyperglycemia). Einhorn et al. (1988) stated that the clinically important effects of diabetes on bone may relate to changes in load bearing capacity, growth, and fracture healing. Decreased mechanical strength has been reported in patients with DM undergoing bone healing (Macey et al., 1989). Though it is difficult to corroborate with evidence that the above changes occur during healing after THA and TKA, it conceptually seems logical that they may do so. Limitations in extrapolating results of experimental DM studies to humans have been pointed out, because most models used simulate total lack of insulin (as seen in type 1 DM) (Funk, Hale, Carmines, Gooch & Hurwitz, 2000).

2.3.3.2 Infection

Patients with diabetes are prone to higher risks of infection (Shah & Hux, 2003; Yang et al., 2001). The risk ratio of an infectious disease in DM cohort versus non-DM was 1.21 (99% CI, 1.20, 1.22) (Shah & Hux, 2003). When infection occurs, loss of metabolic control may occur, which could make resolution of infection very difficult. The issues of metabolic control and infection are so interwoven that Robertson and Polk (1974) questioned whether infection causes DM to be uncontrolled or whether uncontrolled DM is the cause of increased susceptibility to infection. DM has features operating at several levels that increase risk of infection.

Hyperglycemia impairs leukocyte function, which may account for the higher risk of infection in people with diabetes (Goodson & Hunt, 1979). Early studies have shown impaired sticking of leukocytes, decreased migration of leukocytes, and reduced phagocytosis (Robertson & Polk, 1974). Impaired phagocytosis decreases the ingestion of micro-organisms, allowing debris to accumulate and thereby preventing granulation tissue formation (Goodson & Hunt, 1977; Lioupis, 2005). Phagocytosis improves with glucose control, but never returns to normal (Silhi, 1998), leading to the suggestion that inherent defects in the cells occur apart from abnormalities in glucose and insulin concentration. The inability to ingest micro-organisms causes bacteria to continue to colonize and monopolize nutrients and oxygen, thereby decreasing healing

(Terranova, 1991). Gram positive bacteria have also been shown to thrive well in a hyperglycemic environment (Robertson & Polk, 1974).

2.3.3.3 Neuropathy

Diabetic Neuropathy (DN) is one of the complications of diabetes. It refers to symptoms and signs of neuropathy in patients with diabetes in whom other causes of neuropathy have been excluded (Bansal, Kalita, & Misra, 2006). The incidence of DN varies but may be associated with the duration of diabetes. In the largest prospective study published, the incidence of DN at the time of diagnosis of diabetes was 7.5%, increasing to 50%, 25 years after diagnosis (Pirart, 1978). In a prospective complications' study in Europe, the incidence of DN at follow-up among patients without DN at baseline was 23.5% (Tesfaye et al., 2005). Bansal et al. (2006) claimed that two-thirds of patients with diabetes have clinical or sub-clinical neuropathy.

The cause of DN remains unknown, but ischemic and metabolic factors have been implicated (Bansal et al., 2006). Hyperglycemia could increase endothelia vascular resistance, thereby reducing nerve blood flow. The resulting hypoxia leads to capillary damage. Hyperglycemia can cause depletion of nerve myoinositol through a competitive uptake mechanism. Reduced sodium ion gradient decreases the Na^+/K^+ ATPase (sodium/potassium exchanger) activity which results in reduced intracellular myoinositol. The polyol pathway activation leads to the accumulation of sorbitol through the enzyme aldose reductase. The increased accumulation of sorbitol can lead to oxidative stress by increasing the osmotic gradient, causing swelling, leakage and cell membrane breakdown. There is also the activation of protein kinase C and non-enzymatic glycosylation of structural nerve proteins. All the above changes result in abnormal neuronal, axonal and Schwann cell metabolism, leading to impaired axonal transportation (Bansal et al., 2006).

There are many factors reported to be associated with the development of DN. These risk factors include degree of hyperglycemia, duration of diabetes, older age, male gender, and greater than average height. There is also increased incidence of DN in patients with retinopathy or nephropathy (Lipnick & Lee, 1996). In two recent studies, the risk factors for DN were similar to those previously identified, with the addition of some lifestyle related factors. Booya et al. (2005) found a significant relationship between DN and age, gender, degree of diabetes control and duration of diabetes. Tesfaye et al. (2005) found that BMI and smoking were associated with incidence of DN, apart from duration of diabetes, and glycosylated hemoglobin values. The most common type of DN, accounting for about 75%, is distal symmetrical neuropathy (DSN).

Distal symmetrical neuropathy affects large or small nerve fibers. When the large fibers are affected, it is characterized by painless paraesthesia, with impaired vibration, joint position, touch and pressure sensation, and loss of ankle reflex. When the small fibers are affected, there is pain, burning, and impaired pain and temperature sensation (Bansal et al., 2006).

Painful diabetic neuropathy (or neuropathic pain) is a common complication of diabetes. Neuropathic pain is defined as pain initiated or caused by a primary lesion or dysfunction in the nervous system. It is believed that a persistent hyperglycemic state contributes to neuropathy (Bansal et al., 2006). About 10% of patients with diabetes experience persistent pain, which may be spontaneous or stimulus induced, severe or intractable (Bansal et al., 2006). Even the prevalence of neuropathic pain may be higher, between 11-20% (Simmons & Feldman, 2002). Pain is usually worse at night; its description varies and can consist of burning, pins and needles, shooting, aching, jabbing, cramping, tingling, and cold or allodynia (Bansal et al., 2006).

Neuropathic pain impacts significantly on health related quality of life and over 80% of patients with neuropathic pain report moderate to severe pain (Tolle, Xu, & Sadosky, 2006). There is greater deterioration in health status with associated lower (i.e. worse) health utility for these patients (Coffey et al., 2002; McDermott, Toelle, Rowbotham, Schaefer, & Dukes, 2005). Pain severity is significantly related to health state valuation and interference with functioning.

2.3.4 **Effect of DM on Function**

Diabetes Mellitus is often associated with many co-morbid conditions, but the influence of DM on function and independence pose one of the greatest concerns. Patients with DM report greater physical disability than those without diabetes. In a study by Gregg and colleagues, almost 63% of women with DM reported disability on at least one of the physical tasks evaluated compared to 42% of women with no diabetes. In men, the reported disability rates were 39% and 25% respectively for those with and without diabetes (Gregg et al., 2000). In the same study, DM was associated with two-three fold increased odds of not being able to perform physical activities of walking, climbing stairs or doing housework. Even after controlling for co-morbidities, men and women with diabetes had 50% and 46% greater odds respectively of disability compared to those with no diabetes (Gregg et al., 2000).

Similarly, Gregg et al. (2002) in a prospective cohort study of older women with DM noted that the yearly incidence of disability was approximately two times higher in patients with DM compared to non-DM (4.3% for DM and 1.9% for non-DM). Self-reported function and objective performance score (on 6m walk, standing balance and chair stand) were significantly more difficult for persons with DM compared to those without DM. Also, the likelihood of having sub-clinical functional limitation in normal population was found to be higher in persons with DM than without DM (odds ratio = 1.70, 95% CI = 1.40, 2.06). This higher likelihood persisted in an attenuated form (odds ratio = 1.40, 95% CI = 1.14, 1.73) even after controlling for relevant variables in the multivariate analysis (de Rekeneire et al., 2003).

2.4 FUNCTIONAL OUTCOMES

2.4.1 Measuring Functional Outcomes

The increase in healthcare expenditures has prompted the need for consistent evaluation of the effectiveness of medical interventions. Traditionally, the end results of surgical prosthetic intervention have been measured by examining mortality and morbidity rates, operative complications, and survivorships of prosthetic materials (Ethgen, Bruyere, Richy, Dardennes, & Reginster, 2004). Improvements in surgical/medical procedures may be causing these indicators to lose their relevance and no longer reflect healthcare efforts or benefits (O'Boyle, 1992). Recently, health-related outcomes after joint surgeries have been assessed by factors such as economic benefits (Badley & Williams, 1998), changes in pain and mobility (Bellamy, Buchanan, Goldsmith, Campbell, & Stitt, 1988a & 1988b), work disability (Nevitt, Epstein, Masem, & Murray, 1984), and occupation (Johnsson & Persson, 1986). Pain and functional outcomes are very common because they are patients' primary concerns and are also related to independence in activities of daily living.

2.4.2 WOMAC

A disease specific self-administered questionnaire, the Western Ontario and McMaster Universities (WOMAC) Osteoarthritis index, with evaluative and discriminatory properties is one of the outcome tools used to assess disability in hip and knee osteoarthritis (Bellamy, Buchanan, Goldsmith, Campbell, & Stitt, 1988a). Ethgen et al. (2004) reported that the WOMAC was one of the two most commonly used instruments to evaluate outcome post-joint replacement. The WOMAC consists of three subscales with 24 items graded on a five point Likert scale. Items and maximum subscales' scores are as follows: joint pain (five items, maximum score of 20), joint stiffness (two items, maximum score of eight), and joint function (17 items, maximum score of 68). A global score can be calculated by summing the subscale scores (McConnell, Kolopack, & Davis, 2001). A lower score indicates a lower level of symptoms or lower physical disability.

The WOMAC has been used extensively to measure a) joint specific pain, stiffness and function of the hips and knees in patients with osteoarthritis

(Bellamy et al., 1988a & 1988b), b) the effect of physiotherapy regimens (Beaupre, Davies, Jones, & Cinats, 2001; Kramer, Speechley, Borne, Rorabeck, & Vaz, 2004) and c) the effect of surgical interventions (Bellamy et al., 1988a; Fortin et al., 1999; Jones, Voaklander, Johnston, & Suarez-Almazor, 2001, Jones at al., 2003).

The WOMAC has been translated into other languages given its worldwide use (Bae et al., 2001; Soderman & Malchau, 2000; Stucki et al., 1996; Wiegler, Neumann, & Yaron, 1999). The WOMAC has been found to be valid, reliable, and responsive in patient populations with arthritis and after arthroplasty (Bellamy et al., 1988a; Nilsdotter, Roos, Westerlund, Roos, & Lohmander, 2001).

2.4.3 Measurement Properties of the WOMAC

Reliability (test-retest): The initial validation study by Bellamy et al. (1988b) reported the following test-retest reliability coefficients (Kendall's tau c) for the Likert version of the WOMAC: pain (0.68), stiffness (0.48), and physical function (0.68). The visual analog version had the following test-retest values: pain (0.64), stiffness (0.61), and physical function (0.72). In a study to validate the Euro-Qol in patients with osteoarthritis of the knee, the WOMAC was used as a comparative outcome tool, and the reliability scores using Intra-Class Correlation Coefficient (ICC) for the WOMAC pain and function subscales were 0.65 and 0.80 respectively (Fransen & Edmonds, 1999).

The reliability of the physical function subscale is consistently suitable for group comparison and is also found to be suitable for individual client monitoring in clinical practice (Kennedy et al., 2003). It is important to note that the property of a measure to be used for an individual client's evaluation must be superior to those for group use (Goldsmith, Boers, Bombardier, & Tugwell, 1993). Reliability scores of 0.90 and 0.95 are needed for an outcome tool to be used for groups and individual clients respectively (Kennedy et al., 2003). The pain subscale has variable reliability, but it generally meets a minimum standard, while the stiffness subscale has consistently low scores suggestive of poor reliability (McConnell et al., 2001).

Internal consistency: This is a measure of how closely items in a questionnaire measuring the same construct are related. Cronbach's alpha is a measure of internal consistency (McConnell et al., 2001). Bellamy et al. (1988b) reported internal consistency (Cronbach's alpha) for the Likert version of the WOMAC as follows: pain 0.86, stiffness 0.90, function 0.95; and for the visual analog version: pain 0.89, and function 0.89. Kennedy et al. (2003) reported similar results for the internal consistency (Likert version- pain 0.87, stiffness 0.80, and physical function 0.95). Values from other studies suggest that subscales of the WOMAC have internal consistency and thus the items are related to each other (McConnell et al., 2001). The physical function subscale is highly correlated with the total WOMAC score (0.98) and it is therefore an accurate representation of the total score. The pain and stiffness subscales have lower correlation scores with the total WOMAC score (0.85 and 0.65 respectively) (Kennedy et al., 2003).

Responsiveness: Factorial (or structural) validity examines the extent to which domains hypothesized to make up a measure (pain, stiffness and physical function in the case of the WOMAC) actually underlie patients' responses (Stratford & Kennedy, 2004). Studies have shown poor factorial validity for the WOMAC. Kennedy et al. (2003) reported that the physical function subscale failed to detect change in patients with THA and TKA evaluated pre-operation and within two weeks after surgery. The authors concluded that the responses for the WOMAC physical function and pain subscales are not distinct because both are measuring responses about activities. The effect of duplication of activity items on physical function and pain subscales was examined in another study, and the poor factorial validity found was again attributed to this duplication (Stratford & Kennedy, 2004). Generalization of these findings to the WOMAC administered many months after surgery may be limited given the available data (Stratford & Kennedy, 2004). Ryser, Wright, Aeschlimann, Mariacher-Gehler, & Stucki (1999), using a Rasch analysis, concluded that the WOMAC function and pain items seem to represent the same construct. Despite these reports, the WOMAC has been shown to have very good responsiveness.

Responsiveness has been described by using the standardized response mean (SRM), effect size (ES), and relative efficiency (Angst, Aeschlimann, & Stucki, 2001; Kennedy et al., 2003, Nilsdotter et al., 2001). The responsiveness of the WOMAC depends on the intervention being considered. Arthroplasties have large effect sizes, drug interventions have effects ranging from small to large effect sizes, and other treatment regimens (including rehabilitation) have variable effects (McConnell et al., 2001). Effect size with THA was large, ranging from 1.7 to 2.58 (pain), 1.0 to 2.17 (stiffness), and 1.8 to 2.9 (physical function); and the effect sizes after TKA were 0.95 to 41.0 (pain), 0.88 to 24.0 (stiffness), 1.01 to 23.9 (physical function) (McConnell et al., 2001).

Kennedy et al. (2003) reported the Minimum Detectable Change at 90% Confidence Interval (CI) for the WOMAC (Likert version) subscales and the total score as follows: pain (3.19), stiffness (1.57), physical function (6.66), and total score (7.87). The stiffness subscale exhibits the largest error and the physical function subscale the smallest. The SEM reported by Kennedy et al. (2003) may have underestimated the Minimum Detectable Change at 90% CI because the internal consistency data were used. The authors reported that a test-retest reliability coefficient would have yielded a larger Minimum Detectable Change value. A previous study did not find any advantage in terms of the responsiveness of a performance-based measure over the WOMAC, which is a patient self-reported measure (Nilsdotter et al., 2001).

The smallest detectable significant clinical improvement for the WOMAC pain and function subscales was defined as a change of 10/100 units (Ehrich et al., 2000). Criteria for defining improvement for the WOMAC in clinical trials of drug treatment for hip and knee osteoarthritis have been described (Dougados et al., 2000). These criteria were based on pain, function, and global scores. High improvement in pain and function was defined respectively as a change score of 30/100 and 20/100. Moderate improvement was said to have occurred if at least two of the following three criteria were satisfied: (a) a change in pain of 15/100 units (b) a change in function of 10/100 units (c) a change of 10/100 units in the global score (Dougados et al., 2000; Nilsdotter et al., 2003).

Bischoff-Ferrari et al. (2004) divided the WOMAC scores on an interval scale of 0 to 100 into four quartiles and had 50 as a cut-off point for poor functional status. The WOMAC has been shown to exhibit a ceiling effect which may affect its utility among high functioning individuals (Nilsdotter et al., 2003; Ostendorf et al., 2004; Soderman, Malchau, & Herbert, 2001).

2.4.4 Factors that Influence Functional Outcome

Multiple variables likely influence function after TJA and in patients with diabetes. Recognizing patients who may require intensive rehabilitation after TJA has always been a challenge. Predictors of recovery have not been studied as extensively as recovery itself.

Determinants of function after TJA are considered to be broadly dependent on the following factors: peri-operative surgical complications, prosthetic-related factors and non-surgical factors (Bischoff-Ferrari et al., 2004; Jones et al., 2005). Some of the predictors that have been studied and reported include pre-operative function (Fortin et al., 1999; Jones et al., 2003), age (Jones et al., 2001), gender (Fitzgerald et al., 2004; Nilsdotter & Lohmander, 2002), education (Fortin et al., 1999), Body Mass Index (BMI) (Bischoff-Ferrari et al., 2004; Moran, Walmsley, Gray, & Brenkel, 2005), co-morbidity and post-operative complications (Nilsdotter et al., 2003; Fortin et al., 1999). Psychological variables, like expectation for the future, have also gained prominence in functional outcome evaluation (Engel, Hamilton, Potter & Zautra, 2004). When the role of patients' expectations was examined with regards to post-operative functional outcome, expectation of complete pain relief predicted post-operative functional outcomes (Mahomed et al., 2002).

In the DM population, Health Related Quality of Life (HRQOL), including physical function, is related to the determinants of health (Maddigan, Feeny & Johnson, 2004). Determinants of health are divided into three categories: stage of life cycle (age, co-morbidities and complications), subpopulation partitions (gender, education, and income), and sources of heterogeneity (lifestyle e.g. BMI, activity level) (Maddigan et al., 2004).

Stage of life cycle reflects that age, in part, determines an individual's vulnerabilities and susceptibility to disease. When co-morbidities and complications occur with these vulnerabilities, they impact negatively on HRQOL, including function. The sub-population partitions relate to segments across the population where differences in health status exist. Examples of these sources of heterogeneities include gender and socioeconomic status (income, education, etc). The sources of heterogeneity are mechanisms that operate across sub-population partitions and stage of life cycle, and these partly explain differences in health. The sources of heterogeneity are diverse including life style, social determinants of health, activity level, genetics, and differences in access to health care (Maddigan et al., 2004).

2.4.4.1 Baseline Status

Pre-operative WOMAC joint function: Baseline function is by far one of the most consistent predictors of functional outcome after TJA. Fortin et al. (1999) reported that the baseline scores of pain and function were important predictors of the six months scores. These findings were similar to those reported by other authors (Fitzgerald et al., 2004; Holtzman, Saleh, and Kane, 2002a; Jones et al., 2003; Mahomed et al., 2002; Nilsdotter & Lohmander, 2002). The patients with lower function pre-operatively improved with greater margins; however, they never reached the same level as the higher pre-operative functioning group (Fortin et al., 1999; Hajat et al., 2002).

In DM population, early sub-clinical functional limitations have been observed in non-disabled older adults (de Rekeneire et al., 2003). Increased odds of having physical disability among persons with diabetes compared to those without diabetes may represent a differential baseline status in these populations. Gregg et al. (2000) noted increased physical disability in both males and females with diabetes compared to those without, and that baseline functional difficulty was an independent predictor of physical disability in persons with diabetes (Gregg et al., 2002).

Pre-operative pain (WOMAC joint pain and neuropathic pain): Relief of pain is one of the most important post-operative outcomes after TJA. Joint pain improves significantly after TJA (Brander et al., 2003). Heightened pre-operative pain is an independent risk factor for poor outcome post-operatively. Patients with greater pre-operative knee pain (visual analog score > 40) had significantly lower post-operative function at six and 12 months. These patients also used more home care physical therapy and had longer in-patient rehabilitation stays (Brander et al., 2003). Nilsdotter et al. (2003) reported that SF-36 bodily pain pre-operatively predicted function post-operatively. Patients with higher pain had worse

WOMAC function. Similarly, other authors noted that pre-operative WOMAC pain was one of the predictors of post-operative function (Bischoff-Ferrari et al., 2004; Fortin et al., 1999; Holtzman et al., 2002a; Mahomed et al., 2002).

In the DM population, significant baseline pain in the lower extremities may be in the form of neuropathic pain which has been estimated to occur in about 11-20% of patients (Simmons & Feldman, 2002). About 82% of patients with neuropathic pain report moderate to severe pain (Tolle et al., 2006). Pain severity in patients with diabetic neuropathy has been associated with lower health valuation and reported interference with functioning (Coffey et al., 2002; Tolle et al., 2006). Evaluation of the effect of neuropathic pain on the patient may not be adequately captured by the disease-specific WOMAC joint pain subscale. For this, the Health Utility Index may be able to provide additional information on the impact of neuropathic pain on HRQOL (Maddigan et al., 2003a). The single attribute pain score of the Health Utility Index Mark 3 (HUI3), which is a multi-attribute preference-based measure, has been shown to be valid and have adequate responsiveness in patients with TJA (Blanchard et al., 2003 & 2004).

2.4.4.2 Socio-demographic factors

Age: Increased prevalence of co-morbidities in elderly patients may be a reason to assume that functional outcomes will be lower in this age group. There is evidence to suggest, however, that age alone does not limit good functional outcome post THA and TKA (Brander, Malhotra, Jet, Heinemann, & Stulberg 1997; Jones et al., 2001). Jones et al. (2001) reported a comparative functional gain between patients aged 55 to 79 years and those ≥80 years after THA and

TKA. Brander et al. (1997) also studied patients' ≥80 years and a younger age group (65 to79); they concluded that functional outcomes were comparable in both groups, although older patients had more co-morbidity. Laskin (1999) reported that 75% of elderly patients (≥80 years) required the use of a cane for ambulation compared to 18% of patients younger than 85 years after TKA; however, most elderly patients returned to more functional lifestyles after surgery. Hilton, Back, Espag, Briggs and Cannon (2004) used the Knee Society Clinical Function Scores in their comparison study of elderly patients aged > 80 and those aged 60 to 70 after TKA, and found similar functional outcomes in the two groups. In addition, they reported more post-operative complications in the relatively younger age group although the older group had slightly higher length of hospital stay (Hilton et al., 2004). Similarly, Munin, Kwoh, Glynn, Crossett and Rubash (1995) and Forrest, Fuchs, Gutierrez and Girardy (1998) reported that age had an effect on the length of hospital stay and also the need for rehabilitation after joint arthroplasty. In view of good functional outcomes in elderly that are well enough to undergo surgery, Jones et al. (2001) concluded that age alone is not a factor that affects functional outcome.

Age is an important factor in patients with DM too, because as age increases, so does the prevalence of DM and its associated morbid conditions (Mokdad et al., 2003). These co-morbid conditions have been reported to increase the effect of DM in causing functional deficits (de Rekeneire et al., 2003; Maddigan et al., 2005). Apart from co-morbidity, older individuals with DM report more functional difficulty (Gregg et al., 2002).

Gender: Nilsdotter and Lohmander (2002) found no gender-related differences in the post-operative scores of the WOMAC among patients with THA. Fitzgerald et al. (2004) also found similar gains in physical function in both genders after joint arthroplasty. Although men scored higher than women post-operatively, the difference was attributed to higher pre-operative function in men. However, Van Essen, Chipchase, O'Connor and Krishnan (1998) noted gender differences in outcome post TKA. The differences were related to the psychosocial aspects of the patients' general health. In another study that reported outcome on the generic health outcome tool, the SF-36, men were also found to score significantly higher on all subscales of the SF-36, including physical function. These scores were maintained post-operatively at 12 months (Kiebzak, Campbell, & Mauerhan, 2002). Holtzman, Saleh and Kane (2002b) reported that despite improvement in both genders, women were still likely to require assistance at one year for function. Women were however more prone to have osteoarthritis of the hip and knee, and had worse arthritis symptoms and greater disability than men (Hawker et al., 2000). These differences may partly be responsible for the post-operative gender differences in improvement.

In the DM population, women were more likely than men to report physical disability. Gregg et al. (2000) observed that about 63% of women with diabetes reported physical disability compared with 39% of men with diabetes. Also, women performed poorly in objective functional activities such as walking speed, chair stands and standing balance. Women were more likely to have sub-clinical functional limitation among non-disabled older adults than men (de Rekeneire et al., 2003).

Level of education: There have been increasing discussions about the effect of literacy on the health of individuals, as low literacy could affect the use of preventative services, delay diagnoses, reduce understanding of one's condition, reduce adherence to medical instructions and reduce ability to do self-management. Higher level of education has been associated with better short-term functional outcomes after THA and TKA (Fortin et al., 1999 & 2002; Mahomed et al., 2002). Fortin et al. (1999) advised that this factor among others should be considered when evaluating functional outcome after THA and TKA. In a review of patient characteristics that affect the outcome of THA, best functional outcomes were reported for patients with higher educational levels (Young, Cheah, Waddell, & Wright, 1998). Mahomed et al. (2002) also noted that patients with a higher level of education tended to expect better outcomes (pain and physical function), and that expectations predicted outcomes on the WOMAC physical function and pain subscales.

In patients with DM, low literacy has been associated with poor glycemic control (Schillinger et al., 2002). Rothman et al. (2004) reported that patients with poor glycemic control, who received intensive DM management, including education, significantly improved their glycemic control compared to the group who received standard care only. The improvement recorded was more for people with low literacy and less so in people with high literacy. In the low literacy stratum, 42% in the intervention group and 15% in the control group, odds ratio =

4.6 (95% CI = 1.3, 17.2) achieved the glycemic control goal. However, in the high literacy stratum, there was no significant difference in glycemic control (24% in the intervention group and 23% in the control group, odds ratio = 1.0, 95% CI = 0.4, 2.5).

Inadequate health literacy has been linked to the presence of higher rates of certain chronic diseases in people (Wolf, Gazmaranan, & Baker, 2005). Inadequate health literacy was an independent predictor of having DM (odds ratio = 1.48, 95% CI = 1.09, 2.02). People with reduced literacy reported significantly reduced physical function on the SF-36, and were more likely to report difficulty with activities of daily living (odds ratio = 2.83, 95% CI = 1.62, 4.96) and instrumental activities of daily living (odds ratio = 2.25, 95% CI = 1.74, 2.92). Caruso, Silliman, Demissie, Greenfield, and Wagner (2000) reported that lower education was associated with lower function in patients with type 2 DM. Low literacy therefore seems to affect DM control and people with low literacy may also report lower physical function.

2.4.4.3 Life Style and Clinical Factors

Obesity (Body Mass Index): Overweight and obesity are significantly associated with DM and other chronic diseases including high blood pressure, high cholesterol, asthma, arthritis and poor health status (Mokdad et al., 2003). The prevalence of obesity and DM has increased significantly in the last decade (Mokdad et al., 2001). In 2004, 23.1% (5.5 million people) of Canadians ≥18 years were obese and additional 36.1% (8.6 million people) were overweight (Tjepkema, 2005). Obesity (BMI ≥30) in the general US population was 20.9%

in 2001 and 12% in 1991, which was an increase of about 74%. The prevalence rate in 2001 represents a total of about 44.3 million obese US adults (21.4 million men and 22.9 million women). The prevalence of morbid obesity (BMI $\geq$40) and overweight has also increased. The prevalence rate of people with morbid obesity increased from 0.9% in 1991 to 2.3% in 2001, and the percentage of overweight adults in the USA increased from 45% in 1999 to 58% in 2001. In 2000, 2.9% of US adults were both obese and diabetic, compared with 1.4% in 1991 (Mokdad et al., 2001). In 2001, compared with adults with normal weight, those with a BMI $\geq$ 40 had odds ratio of 7.37 (95% CI = 6.39, 8.50) for diagnosed DM (Mokdad et al., 2003). Similarly, among Canadians the prevalence of DM increased with higher BMI; 2.2% in people with normal weight and 12.0% in those with BMI $\geq$ 35 ($p < 0.05$) (Tjepkema, 2005). The likelihood of having DM in obese (BMI $\geq$ 35) Canadian men and women respectively was 7.0 (95% CI = 3.4, 14.4) and 4.4 (95% CI = 2.4, 8.1) (Tjepkema, 2005).

Obesity has been associated with many other health conditions, which ultimately results in significantly increased morbidity and mortality. Patterson, Frank, Kristal, and White (2004) reported that out of 41 health conditions examined in their study, 37 (90%) in women and 29 (70%) in men were associated with increased BMI. In summary, obesity increases risk for many disorders including DM, hypertension, coronary heart disease, dyslipidemia, gall bladder disease, OA, stroke, asthma, sleep apnea, breathing difficulty (obesity hypoventilation syndrome), increased complications of pregnancy, menstrual irregularities, hirtutism, increased surgical risks, psychological distress including depression, and certain malignancies (e.g. prostate, endometrial, uterine, cervical, ovarian, colon, kidney, gallbladder, and post menopausal breast cancer) (Pi-Sunyer, 2002).

Furthermore since obesity is often associated with type 2 DM (Jibodh, Gurkan, & Wenz, 2004; Miric et al., 2002; Mousley, 2003; Namba, Paxton, Fithian, & Stone, 2005), it may contribute to impaired wound healing. Goodson and Hunt (1986) found poor healing in obese mice that were diabetic. Insulin therapy and diet restriction (measures to reduce hyperglycemia) improved healing but did not correct the impairment. The rat models used in this study had diabetes similar to human type 2 DM. This result contrasted with those obtained in rats with DM (type 1) induced by alloxan or streptozotocin in that insulin corrected the healing defects (Goodson & Hunt, 1979). Human type 1 DM also exhibits normal wound collagen accumulation with insulin therapy (Goodson & Hunt, 1984). Goodson and Hunt (1986) concluded that fat accumulation may be an independent factor for impaired healing in obesity-related DM. Fat cells may present a mechanical barrier to inflammatory cell infiltration, fibroblast growth and neo-vascularization. There may also be hypo-perfusion from the multiplicity of blood vessels (Goodson & Hunt, 1986; Mousley, 2003).

Obesity seems to make an independent contribution to deficits in HRQOL regardless of the contributions of associated chronic conditions. A significant association between BMI and reduced physical functioning has been reported (Coakley et al., 1998; Sulander, Martelin, Rahkonen, Nissinen, & Uutela, 2005). Obese men and women had significantly lower scores, an average of 27%

difference, compared to the US norm in a cross-sectional study of male outpatients (Yancy, Olsen, Westman, Bosworth, & Edelman, 2002). Similarly, Lopez-Garcia et al. (2003) observed that obese individuals had a higher frequency of sub-optimal physical function. Trakas, Oh, Singh, Risebrough, and Shear (2001) reported a significantly lower health utility score (on HUI3) as BMI increased in almost all age groups using the Canadian National Population Health Survey of 1996-1997 (except for 30-39 years old male). There was also a trend across increased BMI categories of worsening score in each of the eight single attributes of the HUI3.

There is a significantly higher rate of obesity among patients undergoing joint arthroplasty than in the general population (CJRR, 2005), with markedly increased prevalence among patients having TKA over those having THA (CJRR, 2005; Fitzgerald et al., 2004; Namba et al., 2005). The association of obesity with increased risk of osteoarthritis and possible need for joint arthroplasty (Nevitt, 2002) may be fuelling the concerns that increased weight might have a negative impact on outcomes after joint arthroplasty. However, there are conflicting reports on the effects of obesity on outcome, which may be due to inconsistency in how authors have defined obesity (Jibodh et al., 2004; Namba et al., 2005; Stickles, Philips, Brox, Owens, & Lanzer, 2001), and failure to fully assess the influence of other co-existing morbidities (which may be confounders) in obesity outcome studies (Deshmukh, Hayes, & Pinder, 2002; Moran et al., 2005). The results of the effect of obesity on outcomes are not consistent for short and long term follow-up studies.

Comparable early functional outcomes between patients with and without obesity (defined by using the BMI) have been reported after joint arthroplasty (Deshmukh et al., 2002; Jibodh et al., 2004; Moran et al., 2005; Stickles et al., 2001). Moran et al. (2005) reported that BMI predicted lower Harris Hip Scores (including pain, function and activity) at six and 18 months. Bischoff-Ferrari et al. (2004), using the WOMAC, found that obesity among other things was associated with a worse functional status after THA. Despite similar functional outcomes between patients with and without obesity reported by Stickles et al. (2001), increased BMI was associated with an increased risk of having difficulty ascending and descending stairs at one year post-operation. Available evidence from long term follow-up studies indicated that obesity had a negative effect on functional outcome (Foran et al., 2004b; Foran, Mont, Etienne, Jones & Hungerford, 2004a). Both studies found that patients with obesity had lower scores on the Knee Society Rating Scale.

Depression: Depression has also been associated directly with diabetes (Anderson, Freedland, Clouse & Lustman, 2001) and indirectly through DM-related complications (de Groot, Anderson, Freedland, Clouse, & Lustman, 2001). The prevalence of depression is higher in people with DM compared to those without DM. Approximately 30% of individuals with DM have symptoms of depression and about 11% may be suffering from major depression (Anderson et al., 2001). The odds of having depression are about two-folds in individuals with DM (Anderson et al., 2001; Nichols & Brown, 2001). Individuals with DM are prone to having many chronic conditions (Engum, Mykletun, Midthjell, Holen, &

Dahl, 2005). Likewise, presence of both DM and depression increases the tendency to have even more co-morbid conditions (Black, Markides & Ray, 2003; Egede, 2004; Engum et al., 2005). The presence of chronic conditions in persons with diabetes has often been a confounder in evaluating the specific contribution of DM to some outcome variable of interest. Engum et al. (2005) found that factors associated with depression were similar in persons with or without diabetes. However, the odds of having depression in DM individuals with co-morbid conditions was higher (odds ratio = 1.38, 95% CI = 1.10, 1.74) than the odds in non-DM with co-morbid conditions (odds ratio = 1.16, 95% CI = 1.08, 1.24). Obesity and cardiovascular disease, common conditions in diabetes, have been reported as predictors of having depression in DM individuals (Nichols & Brown, 2003).

Diabetes and depression are commonly associated with significantly increased likelihood of having functional disability (Black et al., 2003; Egede, 2004; Engum et al., 2005). Prevalence of functional disability was as high as 78% in individuals with both DM and depression compared to just 25% in people without these two co-morbid conditions (Egede, 2004). Black et al. (2003) noted that 38% of individuals with both DM and depression reported disability on the modified Katz Activities of Daily Living Scale compared with 14% of people without these co-morbidities. Factors associated with reduced function in people with both DM and depression are presence of co-morbid conditions, age (elderly), female gender, lower income and less than high school education (Egede, 2004).

Patients who had TKA, and presented with significant pre-operative depressive symptoms, had more pain at one year post-operatively (Brander et al., 2003).

Co-morbidity and post-operative complications: The presence of co-morbid conditions in patients undergoing THA and TKA has been associated with reduced short-term functional outcomes (Fortin et al., 1999 & 2002; Mahomed et al., 2002). Jones et al. (2003) reported that number of co-morbid conditions predicted the six-month function after TKA. In a review of patient characteristics that affect the outcome of THA, best functional outcomes were reported for patients without co-morbid conditions (Young et al., 1998). Mahomed et al. (2002) noted that patients with fewer medical co-morbidities tended to expect better outcomes (pain and physical function), and expectations of complete pain relief predicted outcomes for WOMAC physical function. There is probably a complex relationship linking psychological, clinical and demographic predictors of functional outcomes after THA and TKA.

Evaluating the influence of co-morbid conditions on function poses a measurement challenge and the role they play in functional outcomes is not clearly defined. Presently, one of the ways used to measure co-morbid conditions is to generate a summative score of conditions that are identified from a predefined list. Some authors have expressed the opinion that the current method presents a complex construct in a simple manner and the true effects of the conditions may have been diluted (Jones et al., 2005).

Diabetes Mellitus has been shown to be associated with reduced self-reported and performance-based function (Gregg et al., 2000 & 2002; de

Rekeneire et al., 2003; Wu et al., 2003). It is, however, controversial whether DM itself increases the risk of loss of function and independence or if these deficits result more from the accompanying co-morbidity (de Rekeneire et al., 2003). Maddigan, Feeny and Johnson (2005) showed that individuals with deficits in HRQOL, as evaluated with HUI3, had associated co-morbid conditions, and as the number of co-morbid conditions increases, the health utility score decreased proportionally. These authors concluded that the burden of illness in DM was related more to the accompanying co-morbid conditions. Accounting for the effect of co-morbidities attenuates DM's association with reduced function in most of the studies reviewed (Gregg et al., 2000; Maty et al., 2004; de Rekeneire et al., 2003), but significant association persisted. It therefore seems that DM makes a unique independent contribution to the functional deficit that has been reported in people with the disease (DM). However, co-morbidities may have an additive effect in causing reduced function (Wee et al., 2005).

Co-morbidity is one of the factors that have been studied which may influence outcomes in patients after TJA. Previous studies may have underestimated the true effects of co-morbidity as a predictor of functional outcome by using summative scores for co-morbid conditions identified on a predefined list. Evaluating the effect of individual co-morbid conditions on functional outcome may be a better way of assessing their influence. There are many co-morbid conditions, and one whose effect on short-term functional outcome after TJA has not been studied widely is diabetes. Diabetes is important considering its increasing prevalence, especially among the elderly population who are likely to have THA and TKA (Health Canada, 2002; Mokdad et al., 2003).

Co-morbid conditions are predictive of post-operative complications (Jain, Guller, Pietrobon, Bond, & Higgins, 2005; Kreder et al., 2003; Mahomed et al., 2003; Peersman, Laskin, Davis, & Peterson, 2001), and non-homebound discharge locations (Jain et al., 2005). Kreder et al. (2003) reported that patients with a Charlson Index (an index used to measure co-morbidity) of two or more were 2.1 times more likely to have post-operative complications after TKA. Patients with hypertension, diabetes or obesity had an increased likelihood of having post-operative complications after TJA (Jain et al., 2005). Surgical or medical complications during the initial period after surgery can hinder function and joint mobility (Meding et al., 2003).

2.5 SUMMARY STATEMENT

Utilization rates of THA and TKA have been rising and these procedures are common among people aged 65 years and above (CJRR, 2004 & 2005). Many patients are satisfied with their functional outcomes after THA and TKA (Mancuso et al., 1997). Objective outcomes also showed that TJA procedures are very effective (Bachmeier et al., 2001), but an estimated one-fifth to one-third of patients may still have minimal improvement or feel unsatisfied with their outcomes (Nilsdotter et al., 2003). Effort has been exerted in investigating factors that may predict functional outcomes. This could help in identifying patients who may need early intensive rehabilitation to aid functional outcomes. It seems, however, that possible functional outcome predictors are many and knowledge about them is minimal.

One of the factors that could influence functional outcomes is the presence of co-morbid conditions (Fortin et al., 1999). There are methodological challenges in studying the effect of co-morbidity on outcomes of TJA (Jones et al., 2005). Reaching clear conclusions on the effect of co-morbidity on outcomes after arthroplasty has been difficult partly because of the conflicting results of previous studies (Jain et al., 2005). If aggregating chronic conditions together as presently done would dilute the true effects of these conditions on outcomes of TJA, as alluded to by Jones et al. (2005), then studying the effect of a specific condition while controlling for the influence of others may be one way out. Diabetes Mellitus is one condition, with a high prevalence especially among the elderly, whose effect on functional outcomes after TJA has not been widely studied.

Diabetes Mellitus has been shown to be associated with reduced self-reported and performance-based function (Gregg et al., 2000 & 2002; de Rekeneire et al., 2003; Wu et al., 2003). Determining the independent contribution of DM to reduced functional deficits given the prevalence of the associated co-morbidity has been debatable (Maddigan et al., 2005; de Rekeneire et al., 2003). While the debate continues on the relative effect of DM on function in the general population, its effect after TJA has not been studied.

After total joint arthroplasty, studies have shown that patients with diabetes improve functionally, but at a level below that reported for those without diabetes. These studies however focused on long-term clinical and radiological outcomes and did not control for the influence of existing co-morbid conditions and other factors that could influence function (England et al., 1990; Meding et al., 2003; Moeckel et al., 1993; Papagelopoulos et al., 1996; Serna et al., 1994; Yang et al., 2001). It is therefore difficult to determine the independent role played by DM on functional outcomes from these previous studies. Given the high prevalence of DM among elderly patients receiving THA and TKA, it is pertinent to determine the independent effect of DM on the early functional outcomes after these procedures with view to assist in the initial management of patients.

CHAPTER THREE

METHODS

3.1 STUDY OBJECTIVES AND HYPOTHESES

A secondary data analysis of a longitudinal study after primary elective THA or TKA was conducted. The primary objective of this thesis was to determine whether diabetes status (having diabetes or not) is a significant determinant of functional recovery following TJA after adjusting for other potential patient characteristics that could influence function. The secondary objective was to determine whether six-month joint specific function as defined by the WOMAC function subscale scores and effect size of patients with diabetes (DM) differs from those patients without diabetes (NDM) after receiving TJA.

This study aimed to evaluate the following research hypotheses:

1. Diabetes would negatively impact the six-month WOMAC function and effect size post-TJA after controlling for other covariates which could negatively influence function. These include age, gender, education, pre-operative function, pre-operative pain (WOMAC joint pain and Health Utility Index 3- HUI3- single attribute pain scores), BMI, depression, co-morbidities, type of joint operation and post-operative complications.

2a. The six-month post-operative WOMAC physical function scores of patients with DM would be significantly higher (clinically) than the pre-operative WOMAC function scores.

2b. The six-month WOMAC function and the WOMAC function effect size would be significantly higher (clinically) after TJA for patients with NDM than DM.

2c. The pre-operative WOMAC function scores of patients with DM will be significantly lower (clinically) than scores for NDM.

3.2. SUBJECTS

The larger primary study for this thesis was carried out between January 2002 and December 2003. It consisted of a cohort of patients who had THA or TKA at one of the three major hospitals (University of Alberta, the Royal Alexandra and the Misericordia Hospitals) within the Capital Health Region of Alberta (CH). Capital Health, which serves Edmonton and surrounding areas, is one of the nine regional health authorities in the province of Alberta. At the time the primary study was conducted, approximately 1600 THA and TKA procedures were performed annually at the three major hospitals within the CH. The criteria used for inclusion to the primary study were:

- Patients were 40 years of age and older,
- Residence within CH, and
- Ability to speak English.

Patients were excluded if they had hemiarthroplasties, revision, or emergency arthroplasties. Patients who resided in long term care facilities before having joint replacement were excluded because they may represent a small and atypical group of patients who receive joint arthroplasty (Jones et al., 2003).

Eight hundred and eighty-five subjects were eligible for the primary study, out of which 715 agreed to participate. The data on 715 patients who agreed to participate were included in this secondary analysis. A total of 82 participants (11%) were identified as having diabetes. Sixty-six (80.5% of the total DM cases) were identified from the chart and through self-report; 15 were identified from the chart only; and one participant was identified by self-report only. All participants who reported having diabetes or were shown to have diabetes by chart review were considered to have the condition.

3.3. STUDY DESIGN

Patients who were on the health region's joint arthroplasty waitlist were invited to participate. Upon agreement, the participant was interviewed during their pre-admission clinic visit. The baseline interview consisted of questions regarding demographics, medical conditions, pain, function, health status, and social support. The self-reported measures used were the disease specific questionnaire- the WOMAC for pain and function, the Charlson Co-morbidity Index for type and severity of other medical conditions, the Centre for Epidemiologic Studies Depression Scale (CES-D) for depression, the HUI3 for health related quality of life, and ambulatory status.

Follow-up telephone interviews were conducted at six months after surgery using the same outcome measures employed at baseline. Home interviews were conducted for participants who were unable to complete telephone interviews.

Chart reviews were performed after discharge from the hospital to obtain data regarding surgical and peri-operative information including type and number of in-hospital post-operative complications, medical information (such as diabetes status- DM or NDM) and discharge location.

All patients were managed using the health region's clinical pathway for THA and TKA in Capital Health to ensure standardized treatment of medical, pharmaceutical and rehabilitative care over the length of hospital stay. Early mobilization was emphasized in the clinical pathway. Activities of daily living with assistance were commenced on post-operative day one, and active assisted range of motion exercises on post-operative day two (after removal of the hemovac). Patients were assisted to start ambulation by a physical therapist as early as post-operative day one and weight bearing was as tolerated unless otherwise stated (over 95% of participants were discharged with orders of weight bearing as tolerated). Independent ambulation using an assistive walking device was the mobility discharge goal in the protocol.

3.3.1 Sample Size

There is no consensus regarding the calculation of multiple regression sample size (Maxwell, 2000). Sample size in the range of five and 10 times the number of independent variables has been recommended for multiple regression analysis (Maxwell, 2000; Norman & Streiner, 2000). The popular Cohen effect size calculation was also considered (Cohen, 1988). The Cohen formula based on effect size may not give enough power because of the difficulty inherent in accurate determination of multiple regression effect size (Maxwell, 2000).

Sample size calculation for this study was done using the statistical software called Power Analysis and Sample Size (PASS ® 2000). Power Analysis and Sample Size (PASS ® 2000) statistical program approached the sample size calculation from the perspective of power for the overall fit of the model (Hintze, 2000). It incorporates the R–squared change when the variable of interest is added to the model and R–squared of the model with only the control variables in calculating the multiple regression sample size. The PASS ® 2000 program gave an estimated sample size of approximately 309 for an estimated multiple regression model R^2 of 0.20 and an R^2 change of 0.02 with DM status in the model. The sample size calculation based on a similar idea to the PASS ® 2000 statistical program is shown in Appendix 1- Sample size. The sample size needed for Student t-test comparisons for hypothesis two is included in Appendix 1 as well.

3.4 DATA ANALYSIS

3.4.1. Variables

The dependent variables used for the multiple regression analysis in this study were the six-month WOMAC function (primary) and WOMAC function effect size (secondary). Calculation for WOMAC function described later.

The independent variables were age, gender, education, pre-operative function, pre-operative pain (WOMAC joint pain and Health Utility Index 3- HUI3- single attribute pain scores), co-morbidities, BMI, depression, type of joint operation and post-operative complications. Other variables used were ambulatory status, walking aid, weight bearing at discharge, social support and discharge location.

3.4.2 Measurement of variables

WOMAC Function: The WOMAC baseline function, the six-month post-operative function and effect size were assessed using the WOMAC subscales. The six-month post-operative function was the primary dependent variable for the multiple regression analysis. The five-point Likert version (with rating from zero – representing no limitation to four – representing severe limitation) of the WOMAC was used in this study. The physical function subscale has 17 items, with a maximum total score of 68 (Bellamy et al., 1988a and 1988b). Subscale score for function was calculated by simple summation of the assigned items (function = 0 to 68), with higher scores representing more limited function.

The WOMAC administration guideline was followed in the event of missing responses (Bellamy, 1995). A subscale score was not calculated for WOMAC function if four or more questions were missing responses. If only one to three questions were not answered, substitution with the mean of the available items was used. The subscale score for function was transformed to a range from 0-100 points (subject's score ÷ total subscale score) x 100). The WOMAC score was considered a continuous variable on a 0 to 100 interval (higher score meant more disability).

WOMAC effect size was the secondary dependent variable. It was calculated from the difference of the pre- and post-operative WOMAC function scores, divided by the standard deviation of the pre-operative score (Cohen, 1988).

WOMAC Pain: WOMAC joint pain subscale has five items and a maximum score of 20 (Bellamy et al., 1988a and 1988b). The subscale score was calculated by simple summation of the assigned items. The subscale total was calculated if only one item was missing but not if ≥two items were missing. When there was only one missing answer, substitution with the mean of the available responses was used (Bellamy, 1995). The subscale score was transformed to a range from 0-100 points (subject's score ÷ total subscale score) x 100).

Co-morbidity: Twenty three (23) co-morbid conditions identified by the Charlson Co-morbidity Index were used (Charlson, Pompei, Ales, & Mackenzie, 1987). Co-morbid conditions are defined as chronic medical conditions existing before surgical intervention (Jones et al., 2003). The mean number of co-morbid conditions was calculated and the total number of co-morbid conditions was categorized by a summary variable (0 to1, 2 to 3, and 4 or more). The mean number of co-morbid conditions was used in the regression analysis. The summary variable was used to describe co-morbid data. Severity of the co-morbid conditions was not weighted. For co-morbid conditions that are prevalent among patients with DM such as cardiovascular, renal, and ophthalmic problems, both the self-reported and chart review data were evaluated. Because some conditions may be under-reported by patients, presence of any of these conditions either by self-report or chart review was considered a positive finding.

Health Utility Index 3 (HUI3) Pain: Pre-operative pain was also assessed using the HUI3 single attribute pain score (see HUI3 psychometric properties below) to account for neuropathic pain commonly seen in patients with diabetes. The HUI3 as a Health Utility measure gives information which the disease specific measure for OA may not provide especially in conditions like diabetes (Maddigan et al., 2004).

HUI3 is a multi-attribute measure which can provide information on specific attributes (single attributes utility score- SAUS) of health in addition to the overall index score (Maddigan et al., 2005). Each single attribute can have a score ranging from 0.0 to 1.0 (0.0 represents the lowest functioning level and 1.0 represents full functioning capacity).

Preliminary evidence of the construct validity of the HUI3 in type 2 DM has been provided (Maddigan, Feeny, Johnson, 2003b), and as well as a population-level construct validity in people with arthritis (Grootendorst, Feeny & Furlong, 2000). HUI3 is also valid in patients with OA needing THA (Blanchard et al., 2004). HUI3 is not as responsive as the disease-specific measures in THA, but the overall score and the single attribute scores could provide additional valuable information.

Socio-demographic factors

Age: was calculated as the number of years since birth to the last birthday before data collection. Age was also considered as a dichotomous variable (≤65 or ≥65).

Gender: was categorized into male or female.

Education: was recorded as the highest level of education completed, and was categorized into: less than high school education, and high school and more than high school education (non-university and university degrees).

Body Mass Index (BMI): BMI was calculated from the weight and height data reported in the chart. Obesity has been defined as BMI ≥30 (Foran et al., 2004b; Moran et al., 2005). BMI was used as a continuous variable, but a categorical BMI was also evaluated (Normal weight = BMI of up to 24.9, Overweight = BMI between 25 and 29.9 and Obesity = BMI ≥30).

Depression: Centre for Epidemiologic Studies Depression Scale (CES-D) was used to assess depression. It has been found to be reliable and valid when used among elderly. The scale has 20 items and each item is scored on a four-point ordinal level; thus the total score could range from 0 to 60. The total score was computed by summation of the 20 item scores. If more than four questions have missing answers, CES-D was not scored and the case was excluded. For patients with four or less missing answers, the mean derived from questions with scored items was substituted for questions with missing items (Radloff, 1977). Positive items (items 4, 8, 12 and 16) were reversed so that they were similar to the remaining questions.

A score of ≥16 on the CES-D is categorized as depression and scores of 0 to 15 as no depression. For this study, a cut off score of 16 was used to categorize patients into two groups (depression absent = CES-D score of 0-15, and depression present = CES-D score ≥16) (Radloff, 1977).

The CES-D has good internal consistency with an alpha of 0.85 in the general population and 0.90 for the psychiatric population. It has satisfactory test-retest reliability over a two to eight week period ranging from 0.51 to 0.67 (Hann, Winter & Jacobsen, 1999). Using the CES-D cut-off score of ≥16 has been shown to have high sensitivity (100%) and specificity (88%) for depression in the previous month in a community based sample of older adults between the ages of 55 and 85 years (Beekman et al., 1997).

Surgical Variables

Post-operative complications: number of post-operative complications was categorized by a summary variable (zero, one, and two or more) (Fitzgerald et al., 2004).

Peri-operative variables: (1) Ambulatory status at admission was quantified by the maximum distance participants could walk using their usual walking aid. The walking aid needed to walk was noted (e.g. cane, crutches, or walker). Participants also indicated factors that limited walking such as pain/discomfort, and fatigue. Weight bearing status was the weight bearing order recorded at discharge (e.g. full, partial, feather, non-weight bearing). (2) Demographic: social support was quantified by (a) the marital status at admission (e.g. married, common law, single, widowed, separated, and divorced) and (b) who lived with the participant (lived alone, spouse, children etc).

3.4.3. Paired and Independent Comparisons

Paired t-test was used to compare the pre-operative and six-month post-operative WOMAC function scores of patients with DM. An independent t-test was used to compare the six-month post-operative WOMAC scores and effect size for WOMAC function between patients with DM and NDM after TJA.

3.4.4. Regression Analyses

Despite reported differences in functional outcomes for THA and TKA (Bachmeier et al., 2001), a separate model for THA for the regression analysis could not be done because of small sample size for patients with DM who had THA. Joint type was thus included as one of the independent variables.

Univariate analysis: Univariate analysis was done for each independent variable on the dependent variables (six-month WOMAC physical function score and the effect size for WOMAC function). The main variable of interest in this study was diabetes status and the covariates that were controlled for included age, gender, education, pre-operative function, pre-operative pain (WOMAC joint pain and HUI3 single attribute pain scores), BMI, depression, co-morbidities, type of joint operation and post-operative complications.

Interaction Regression Models: intermediate analyses were also done to assess for interactions. Based on the literature and clinical relevance, the following interaction terms were developed and assessed: Diabetes status coupled with each of these variables: Body Mass Index (BMI), baseline WOMAC pain, HUI3 SAUS, co-morbidity, depression, and in-hospital complications. For example, the interaction models for diabetes status and BMI had the following three variables in the model: diabetes status, BMI and the interaction term of diabetes status and BMI. The model therefore had two main effects and one interaction effect. Significant main and interaction effects at this level of analysis were put into the multiple regression models. Clinical meaningfulness or the achievement of p ≤ 0.25 for the univariate and interaction analyses (Hosmer & Lemeshow, 2000) was used as the conditions for including independent (primary covariates) variables in the multivariate analysis.

Multiple Linear Regressions: Multiple linear regressions were done to examine the independent association of diabetes status with function. Two separate models were developed, one for the six-month WOMAC function and another for the effect size for WOMAC. Age, gender, type of joint operation, and DM status were forced into the regression models containing the other covariates. A forward selection was used and the stability of the final model was checked by running another regression analysis using the backward selection method.

Regression model diagnostics were done to verify that the assumptions of linearity, independence, normality and equal variances for multiple regression were not violated (e.g. using residual scatter plots and histograms, and the Durbin-Watson statistic) (Fox, 1991).

Correlation matrixes, tolerance, and the Variance Inflation Factor (VIF) statistics of all independent variables were inspected to evaluate for multicollinearity. VIF is an index of how much variance of the regression coefficients are inflated because of multi-collinearity (Norman & Streiner, 2000). Tolerance on the other hand is also related to VIF and it is calculated as the reciprocal of VIF (1/VIF). Correlation of > 0.75 between two independent variables indicated possibility of collinearity (Kleinbaum, Kupper, Muller, & Nizam, 1998). The acceptable values for the tolerance and the VIF are > 0.2 and < 10 respectively (Norman & Streiner, 2000).

The case-wise diagnostics were done to assess for influential cases that could unduly influence the multiple regression models. The Cook's distance statistics for cases with standardized residuals greater than ±2 were assessed. The Cook's distance measures the influence of an observation and how much the regression coefficients change if the observation was deleted (Kennedy et al., 2006). An observation with Cook's distance of >1 deserves closer scrutiny; if the model is correct, the Cook's distance should be less than 1 (Kennedy et al., 2006). Other case-wise diagnostics statistics inspected were the average leverage and the mahalanobis distance.

The Statistical Package for the Social Sciences (SPSS), version 13, was used for the data analyses (SPSS Inc, 2004). Statistical significance was set at $p \leq 0.05$ for all the tests and all statistical tests were 2-tailed.

CHAPTER FOUR

RESULTS

4.1 SUBJECTS' CHARACTERISTICS

4.1.1 Participants

Seven hundred and fifteen (80.8%) of 885 eligible subjects participated in this study. For the primary analysis using the WOMAC function subscale, the subject inclusion and exclusion to the study is illustrated in Figure 1 (Appendix 2). Nine (1.3%) subjects were excluded at baseline (Five had completely missing data for baseline WOMAC questions and four subjects skipped more questions than allowed for function subscale). None of the excluded subjects at baseline had diabetes. At six months follow-up, 78 (10.9%) subjects were excluded (76 had completely missing data for the WOMAC questions and two subjects skipped more questions for the function subscale than allowed in the WOMAC administration guideline). Ten of the subjects excluded at six months post-operatively had diabetes. Overall, 706 (98.7%) and 628 (87.8%) of the initial 715 subjects had valid data at baseline and six months respectively (Appendix 2, Table 1). The number of subjects with paired function scores (pre- and six months post-operation) was 621 (therefore seven subjects just had scores for only the baseline or six-month post-operation periods). Eight additional subjects were excluded because of missing data for one or more independent variables for the multivariate analyses. Therefore, the primary analysis is based on 613 subjects with valid data at baseline and at six months post-operatively.

For the 715 participants, 82 (11.5%) had diabetes (DM). For joint type, 408 (57%) of the participants had TKA. The characteristics of the participants are presented in Table 4-1. Further analyses and results were presented for participants based on their diabetes status.

4.1.2 Non-Participants in the Study

Of the 885 participants with elective THA or TKA eligible for the primary longitudinal cohort study, 170 (19.2%) refused to participate. The mean age of all the non-participants was 69 years (SD = 10.8) and 96 (56.5%) of them were female. The non-participants were slightly older than the participants at 69 (SD = 10.8) versus 67 years (SD = 10.4) (p = 0.01, 95% CI = -4.10, -0.56). There were no other demographic differences noted between the non-participants and the final study sample with respect to gender (p = 0.38), and the type of joint replaced (p = 0.49). The characteristics of non-participants by the type of joint operated are presented in Appendix 2 (Table 2).

4.1.3 Baseline Demographics by DM Status

Baseline demographic characteristics are presented in Table 4-1. The majority of the participants did not have diabetes (NDM) (n = 633, 88.5%). Among the 82 (11.5%) participants with DM, 44 (53.7%) were females, mean age of 67years (SD = 9.5), with majority undergoing TKA (n = 61, 74.4%). Due to small sample size for DM participants with THA, results are presented as one group (Total Joint Arthroplasty- TJA) for NDM and DM and for TKA separately. There were no differences in the demographic characteristics between NDM and DM for TJA with regards to age (p = 0.68, 95% CI = -2.92, 1.90), gender (p =

0.20), education (p = 0.12), social support by both marital status (p = 0.47) and who lives with participant (p = 0.21). For participants with TKA, the demographic differences were not significant (age, p = 0.40, 95% CI = -1.62, 4.07; gender, p = 0.20; education, p = 0.37; marital status, p = 0.98; who lives with participant, p = 0.74).

Table 4-1: Patient characteristics

	TJA		TKA	
Characteristics	NDM (n= 633)	DM (n= 82)	NDM (n= 347)	DM (n= 61)
Demographics				
Age (yr) mean (SD)	66.7 (10.6)	67.2 (9.5)	67.7 (10.5)	66.5 (10.2)
Female, n (%)	386 (61.0)	44 (53.7)	218 (62.8)	33 (54.1)
Living alone, n (%)	146 (23.1)	24 (29.3)	84 (24.2)	16 (26.2)
Married, n (%)	434 (68.6)	53 (64.6)	228 (65.7)	40 (65.6)
At least high school education, n (%)	517 (81.7)	61 (74.4)	274 (79.0)	45 (73.8)
Medical status				
Primary Osteoarthritis, n (%)	574 (90.7)	77 (93.9)	323 (93.1)	56 (91.8)
Co-morbid conditions* mean (SD)	3.08 (2.0)	3.55 (2.0)	3.27 (2.0)	3.46 (2.0)
Depression present, n (%)	122 (19.6)	13 (16.0)	60 (17.6)	9 (14.8)
Body Mass Index* (kg/m^2), mean (SD)	30.86 (6.4)	34.15 (6.4)	31.66 (6.3)	34.43 (6.8)
Surgical, n (%)				
Implant fixation				
Cementless			78 (23.4)	13 (22.0)
Hybrid			74 (22.2)	15 (25.4)
Cemented			181 (54.4)	31 (52.5)
In-hosp. comp., None, n (%)	422 (66.7)	46 (56.1)	232 (66.9)	36 (59.0)
Health services utilization				
Discharge Location* Home, n (%)	388 (64.3)	39 (52.0)	205 (61.0)	28 (50.9)

* = significant at P <0.05 for TJA. TJA = Total Joint Arthroplasty, TKA = Total Knee Arthroplasty, In-hosp. comp = In-hospital complications.

4.2 FUNCTION

4.2.1 Baseline WOMAC Pain, Stiffness, Function and Health Utility Index Pain

Table 4-2 presents the mean and standard deviation for the baseline WOMAC and HUI3 pain, WOMAC stiffness and function for NDM and DM participants. Independent student t-test showed that there were no significant differences in baseline WOMAC pain (p = 0.68, 95% CI = -4.91, 3.22), HUI3 pain (p = 0.25, 95% CI = -0.03, 0.12), WOMAC stiffness (p = 0.86, 95% CI = -5.32, 4.41) and WOMAC function (p = 0.43, 95% CI = -5.79, 2.48) between NDM and DM for all participants.

There were no differences in the baseline WOMAC and HUI3 pain between NDM and DM participants who were undergoing TKA, WOMAC pain (p = 0.86, 95% CI = -5.24, 4.38), WOMAC stiffness (p = 0.89, 95% CI = -6.21, 5.42), WOMAC function (p = 0.17, 95% CI = -8.21, 1.45), and HUI3 pain (p = 0.08, 95% CI = -0.009, 0.161).

4.2.2 Baseline Walking Ability, Aid required to Walk and Factors Limiting Walking

Table 4-3 presents the baseline walking ability, use of walking aid and factors limiting walking. Baseline walking distance was limited for most participants with walking one to five blocks being the distance reported by about 42% of NDM and DM participants. There was a significant difference in the distance participants were able to walk between NDM and DM at baseline for

TJA (p = 0.03), but not for TKA participants (p = 0.32). More than half of NDM and DM participants required an assistive device to walk.

Pain and discomfort was the most frequently cited factor limiting walking in all participants. There were no significant differences in the type of support required for walking (p = 0.27 for TJA and p = 0.79 for TKA participants) and factors limiting walking between groups (p = 0.27 for TJA and p = 0.42 for TKA participants).

Table 4-2: Pre-operative health status

	TJA		TKA	
Variable, (n) mean (SD)	NDM	DM	NDM	DM
HUI3 pain	(632) 0.49 (0.33)	(82) 0.44 (0.34)	(347) 0.55 (0.31)	(61) 0.47 (0.32)
WOMAC pre-operative pain	(623) 51.84 (17.4)	(82) 52.68 (19.0)	(340) 48.91 (17.4)	(61) 49.34 (18.8)
Pre-operative joint stiffness	(627) 51.99 (20.7)	(82) 52.44 (23.9)	(343) 50.22 (20.5)	(61) 50.61 (25.1)
Pre-operative function	(624) 48.74 (17.8)	(82) 50.39 (18.6)	(340) 44.11 (17.4)	(61) 47.49 (19.0)

WOMAC indicates Western Ontario and McMaster Universities Osteoarthritis Index, HUI3, Health Utility Index Mark 3, TJA = Total Joint Arthroplasty, TKA = Total Knee Arthroplasty, NDM = Non-diabetes, DM = Diabetes.

Table 4-3: Baseline walking ability, use of walking aid and factors limiting walking

	TJA		TKA	
Characteristics, n (%)	NDM (n=633)	DM (n=82)	NDM (n=347)	DM (n=61)
Walking distance				
Indoors	73 (11.6)	19 (23.2)	38 (10.9)	11 (18.0)
< 1 block	170 (26.9)	15 (18.3)	84 (24.2)	12 (19.7)
1-5 blocks	264 (41.8)	35 (42.7)	147 (42.4)	26 (42.6)
6-10 blocks	76 (12.0)	9 (11.0)	47 (13.5)	9 (14.8)
Unlimited	49 (7.8)	4 (4.9)	31 (8.9)	3 (4.9)
Assistive walking device				
None	299 (47.4)	32 (39.5)	183 (53.0)	29 (48.3)
Walker	70 (11.1)	13 (16.0)	28 (8.1)	5 (8.3)
Others (canes & crutches)	262(41.5)*	36 (44.4)	134(38.8)*	26 (43.3)
Factors limiting walking,				
None	11 (1.7)	0 (0.0)	6 (1.7)	0 (0.0)
Pain/discomfort	556 (87.8)	70 (85.4)	303 (87.3)	52 (85.2)
Fatigue/others	66 (10.4)	12 (14.6)	38 (11.0)	9 (14.8)

* Six non-DM pts for all cases (1.0%) and 6 non-DM pts with TKA (1.7%) were using wheelchair for mobility, TJA = Total Joint Arthroplasty, TKA = Total Knee Arthroplasty.

4.2.3 Functional Outcomes Post-Operatively

4.2.3.1 Six-Month Post-operative WOMAC Function

The mean and standard deviation for the six-month post-operative WOMAC function are shown in Table 4-4. Comparison of the six-month WOMAC function scores showed that NDM had a better score for TJA (p = 0.02, 95% CI = -9.56, -1.00) and TKA participants (p = 0.01, 95% CI = -10.78, -1.29). The differences at six months for TJA and TKA participants were not up to the

10-points considered to be the minimum clinically important difference (Ehrich et al., 2000).

At baseline, the majority of participants had moderate to severe difficulty with all of the functional tasks assessed by the WOMAC function subscale, except for two tasks (lying in bed and sitting). For lying in bed and sitting, between 45% and 48% still had moderate to severe difficulty (Table 3- Appendix 2). At the six-month post-operative period, functional tasks on WOMAC presented only mild or no difficulty to participants. Table 4 (Appendix 2) presents the percentage of participants who still had moderate to severe difficulty with some functional activities at 6 months post-operatively. The majority of the NDM and DM participants had moderate to extreme difficulty doing heavy domestic duties.

4.2.3.2 **Change in Function**

The mean and standard deviation for the six-month absolute WOMAC function scores and the change scores (pre-operative minus six-month WOMAC function scores) are shown in Table 4-4. A paired t-test was used to test within NDM and DM groups separately for the difference between pre-operative and six-month scores. There were significant differences in the change scores for NDM and DM participants (NDM: $p < 0.001$, 95% CI = 28.94, 32.13; DM: $p < 0.001$, 95% CI = 22.97, 33.04).

An independent t-test done to compare NDM and DM for change in WOMAC scores did not show any difference for TJA ($p = 0.30$, 95% CI = -2.23, 7.29) and for TKA participants ($p = 0.72$, 95% CI = -4.64, 6.67). Standardized change scores in the form of effect sizes were shown in Table 4-4. Effect sizes were fairly similar and comparison between NDM and DM showed no significant difference for TJA (p = 0.33, 95% CI = -0.41, 0.14) and TKA participants (p = 0.58, 95% CI = -0.42, 0.24).

Table 4-4: Post-operative WOMAC function

	TJA		TKA	
Variable	NDM (n= 556)	DM (n= 72)	NDM (n= 299)	DM (n= 52)
Six-month function,* mean (SD)	18.54 (14.3)	23.90 (17.5)	18.78 (15.6)	24.89 (18.6)
	n= 549	n= 72	N= 293	n= 52
Change score**	30.53	28.00	25.23	24.21
Effect Size†, mean (SD)	1.74 (1.1)	1.61 (1.2)	1.47 (1.1)	1.38 (1.2)
Change score ≥10 Points (n, %)	467 (85.1)	59 (81.9)	229 (78.2)	39 (75.0)

*Significant at $p < 0.05$. **change score calculated as preoperative minus six-month score. † Effect size was calculated as the preoperative score minus the six-month score, divided by the SD of the preoperative score. WOMAC indicates Western Ontario and McMaster Universities Osteoarthritis Index, TJA = Total Joint Arthroplasty, TKA = Total Knee Arthroplasty, NDM = Non-diabetes, DM = Diabetes.

4.3 INDEPENDENT VARIABLES

4.3.1 Body Mass Index (BMI)

The mean and standard deviation for BMI were presented in Table 4-1. Participants with DM had higher BMI than non-DM for participants with TJA and TKA (TJA: p < 0.001, 95% CI = -4.77, -1.82; TKA: p = 0.002, 95% CI = -4.52,-1.03). The mean BMI scores for participants with TJA and TKA were greater than

$30 Kg/m^2$, the cut off score for obesity, this implied that most participants were either overweight or obese.

4.3.2 Co-morbid Conditions

The mean number of co-morbid conditions reported was 3.1 (SD = 2.0) and 3.6 (SD = 2.0) respectively for NDM and DM participants (p = 0.04, 95% CI = -0.92, -0.01) (Table 4-1). The number of co-morbid conditions were not different for participants with TKA (p = 0.51, 95% CI = -0.74, 0.37). For TJA and TKA participants, those reporting two or more co-morbid conditions were not different between the NDM (n = 491, 77.6% and n = 280, 80.7%) and DM groups (n = 71, 86.6% and n = 53, 86.9%) (p = 0.06 and p = 0.25 respectively). Table 5 in Appendix 2 presents the frequency at which co-morbid conditions were cited by NDM and DM participants. The top two co-morbid conditions for patients with and without DM were high blood pressure (DM = 57 (69.5%), NDM = 279 (44.1%), and chronic low back pain (DM = 32 (39%), NDM = 222 (35.1%).

4.3.3 Depression

Table 4-1 presented the number of participants with depression (depression present or absent based on cut off score of ≥16 on the CES-D scale) for NDM and DM participants. Based on the CES-D depression scores, less than one-fifth had depression in both NDM and DM groups. There were no significant differences between DM and NDM participants (p = 0.45 for TJA and p = 0.59 for TKA).

4.3.4 **Post-Operative Complications**

In-hospital complications were present in 211 (33.3%) of NDM and 36 (43.9%) of DM participants (TJA). The number of participants with no complication, one, and two or more complications were not different for NDM and DM groups (p = 0.15 for TJA, p = 0.47 for TKA participants). The three frequent in-hospital complications among NDM participants were urinary tract infection (n = 19, 3.0%) and joint and wound infection (n = 16, 2.5%). And among DM participants, the three frequent complications were joint and wound infection (n = 4, 4.9%) and congestive heart failure (n = 2, 2.4%).

Table 4-5 presents the percentage and number of participants with different in-hospital complications. Overall, not many participants had in-hospital complications. Complications typically due to DM status were not present in high number in this study, for example, joint and wound infections, and other cardiovascular events. Many of the complications were minor, but one patient with TKA had ventricular tachycardia and another had coronary artery bypass. One other patient with THA had a cardiac arrest and died post-operatively.

Table 4-5: Participants with presence of in-hospital complications

	TJA		TKA	
In-hospital complications	NDM	DM	NDM	DM
Device Related, n (%)				
Joint or wound infection	16 (2.5)	4 (4.9)	11 (3.2)	4 (6.6)
Device refracture	2 (0.3)	0 (0.0)	0 (0.0)	0 (0.0)
Urinary, n (%)				
UTI	19 (3.0)	0 (0.0)	14 (4.0)	0 (0.0)
Urinary retention	5 (0.8)	1 (1.2)	4 (1.2)	0 (0.0)
Cardiac n (%)				
Myocardiac infarction	3 (0.5)	1 (1.2)	3 (0.9)	1 (1.6)
CHF	1 (0.2)	2 (2.4)	1 (0.3)	1 (1.6)
Pulmonary, n (%)				
Pneumonia	1 (0.2)	1 (1.2)	0 (0.0)	1 (1.6)
Pulmonary embolism	2 (0.3)	0 (0.0)	2 (0.6)	0 (0.0)
Pulmonary edema	2 (0.3)	1 (1.2)	2 (0.6)	1 (1.6)
Bleeding/thrombus/others, n (%)				
GIT bleed	1 (0.2)	0 (0.0)	1 (0.3)	0 (0.0)
DVT	3 (0.5)	0 (0.0)	3 (0.9)	0 (0.0)

None of the participants had the following in-hospital complications: dislocation, loss of bone reduction-device or bone complications, stroke, and sepsis. UTI = urinary tract infection, CHF = congestive heart failure, GIT = gastro-intestinal tract, DVT = deep vein thrombosis.

4.4 MULTIVARIATE ANALYSES

4.4.1 Univariate Analyses

Tables 4-6 and 4-7 present the regression coefficients for the six-month and effect size for the WOMAC function. Diabetes status had a significant linear association with the six-month WOMAC function ($p = 0.004$) but not with effect size. For the six-month WOMAC function and effect size, most of the independent variables achieved the set probability level ($p \leq 0.25$) and were included in the multiple regression models. Other independent variables were included in the multiple regression models based on clinical significance.

4.4.2 Interaction Regression Models

Table 4-8 presents the regression coefficients for the interaction terms for variables considered to likely have interaction with diabetes status. None of the interaction terms for WOMAC effect size achieved the probability level to merit further consideration. For the six-month WOMAC function model, only the interaction term for diabetes status and depression (p = 0.15) was included in the final multiple regression model.

Table 4-6: Univariate Regression Coefficients for the Six-month WOMAC Function

Variables	b	SE	95% CI	P
Baseline wopa	0.196	0.034	0.130, 0.263	<0.001
Baseline wofu	0.249	0.032	0.185, 0.313	<0.001
Baseline SAU	-7.920	1.787	-11.430, -4.411	<0.001
Gender, Male	-0.756	1.209	-3.131, 1.619	0.532
Age	1.795	1.204	-0.569, 4.158	0.136
Educ.	-3.052	1.530	-6.057, -0.047	0.047
Co-morb.	1.238	0.291	0.667, 1.810	<0.001
BMI	0.181	0.092	0.001, 0.361	0.049
Comp. 1	1.514	1.299	-1.038, 4.065	0.245
Comp. 2	4.308	1.796	0.781, 7.835	0.017
Depress.	6.521	1.479	3.616, 9.426	<0.001
Joint, Knee	1.181	1.191	-1.158, 3.519	0.322
DM, present	5.277	1.845	1.653, 8.901	0.004

Wopa = WOMAC pain, wofu = WOMAC function, SAU= Health Utility Index 3 Single Attribute pain, Educ = high school and above education, co-morb = sum of co-morbid conditions, comp. 1 = one in-hospital complication, comp. 2 = two or more in-hospital complications, b = unstandardized beta coefficient, SE = standard error, CI = confidence interval.

Table 4-7: Univariate Regression Coefficients for the WOMAC Function Effect Size

Variables	b	SE	95% CI	P
Baseline wopa	-0.032	0.002	-0.037, -0.028	<0.001
Baseline wofu	-0.043	0.002	-0.047, -0.039	<0.001
Baseline SAU	1.188	0.127	0.938, 1.439	<0.001
Gender, Male	0.362	0.090	0.186, 0.538	<0.001
Age	0.301	0.090	0.126, 0.477	0.001
Educ.	-0.131	0.115	-0.357, 0.095	0.255
Co-morb.	0.023	0.022	-0.021, 0.066	0.307
BMI	0.001	0.007	-0.012, 0.015	0.879
Comp. 1	0.006	0.098	-0.186, 0.198	0.948
Comp. 2	0.076	0.135	-0.190, 0.342	0.577
Depress.	-0.258	0.113	-0.480, -0.036	0.023
Joint, Knee	0.664	0.085	0.496, 0.831	<0.001
DM, present	0.135	0.139	-0.137, 0.407	0.329

Wopa = WOMAC pain, wofu = WOMAC function, SAU = Health Utility Index 3 Single Attribute pain, Educ = high school and above education, co-morb = sum of co-morbid conditions, comp. 1 = one in-hospital complication, comp. 2 = two or more in-hospital complications, b = unstandardized beta coefficient, SE = standard error, CI = confidence interval.

Table 4-8: Multiple Linear Regression for Interaction Models

	Six-month WOMAC			Effect Size		
Interaction Variable	b	SE	P	b	SE	P
DM X BMI	0.117	0.305	0.701	0.002	0.023	0.924
BMI	0.129	0.098	0.186	<0.001	0.007	0.971
DM	0.830	10.497	0.937	0.062	0.789	0.938
DM X HUI3 pain	-1.105	5.471	0.840	-0.316	0.389	0.417
HUI3 pain	-7.507	1.902	<0.001	1.239	0.136	<0.001
DM	5.289	2.989	0.077	0.346	0.213	0.105
DM X wopa	0.076	0.112	0.500	0.006	0.007	0.422
Wopa	0.184	0.036	<0.001	-0.033	0.002	<0.001
DM	0.709	6.343	0.911	-0.099	0.421	0.814
DM X co-morbid	-0.649	0.886	0.464	-0.048	0.067	0.478
Co-morbidity	1.256	0.311	<0.001	0.027	0.024	0.258
DM	6.978	3.667	0.057	0.295	0.279	0.290
DM X depression	7.049	4.835	0.145**	0.395	0.369	0.285
Depression	5.883	1.553	<0.001	-0.297	0.119	0.013
DM	3.640	2.005	0.070	0.040	0.153	0.792
DM X comp. 1	-2.088	4.250	0.623	0.081	0.320	0.801
DM X comp. 2	-3.138	4.840	0.517	-0.360	0.365	0.324
In-hosp. comp. 1	1.666	1.368	0.224	-0.004	0.103	0.966
In-hosp. comp. 2	4.292	1.978	0.030	0.130	0.150	0.387
DM	6.230	2.738	0.023	0.180	0.206	0.384

** Interaction variable included in the multiple regression model, Wopa= baseline WOMAC pain, HUI3 Pain = Health Utility Index 3 Single Attribute, Co-morbidity = sum of co-morbid conditions, Comp. 1 = one in-hospital complication, Comp. 2 = two or more in-hospital complications, b = unstandardized beta coefficient, SE = standard error.

4.4.3 Multiple Linear Regressions

Two models were developed, one each for the six-month and effect size for WOMAC function as the dependent variable. WOMAC and HUI3 pain scores were entered as two independent variables in the multiple regression models. The correlation between the two pain subscales was not high enough (r = -0.55) to be considered collinear, suggesting they were measuring different parameters (i.e. correlation < 0.75, Kennedy et al, 2006). Appendix 2- Table 6

Table 4-9 presents the coefficients for the final multiple regression model with six-month WOMAC function as the dependent variable. Twelve variables were introduced into this model, including diabetes status, and one interaction term for diabetes status and depression. Only seven variables were included in the final model, these included diabetes status, age, gender, joint type, baseline WOMAC function, depression, and co-morbidity. The variables entered into this model accounted for 13% of the explained variance for the six-month WOMAC function (Table 4-9).

Diabetes status had a significant linear relationship with the six-month WOMAC function at the univariate level (p = 0.004, 95% CI = 1.65, 8.90). But in the multiple regression model controlling for the other variables considered in this study, diabetes status was not a significant variable (p = 0.11, 95% CI = -0.62, 6.32). The independent predictors of the six-month WOMAC function were baseline WOMAC function, depression, co-morbidity and the type of joint operated. Age had a trend towards significance. The baseline WOMAC function was the most influential variable predicting the six-month WOMAC function with standardized coefficient of 0.30. Every 10-points increase in baseline WOMAC function was associated with 2.6 increase in the six-month WOMAC function. Co-morbidity has standardized coefficient of 0.11 and for every one point increase in mean number of co-morbid conditions, there is about one-point reduction in the six-month WOMAC function.

The effect of the top six co-morbid conditions and three complications (instead of the mean co-morbid score and the in-hospital complication categories) were checked on the six-month WOMAC function. The co-morbid conditions included circulatory disease, high blood pressure, heart disease, kidney disease, eyes problem, and chronic low back pain. The in-hospital complications selected were joint and wound infection, urinary tract infection, and congestive heart failure. The regression parameters were not better than the reported model using mean co-morbid score and in-hospital complication categories (Appendix 2, Table 7)

Table 4-9: Multiple Linear Regression (Forward selection) for Six-month WOMAC Function

Variable	b	Standard-Ized β	95% CI	Partial r	P
Intercept	-0.834				0.727
Diabetes Status	2.854	0.062	-0.62, 6.32	0.07	0.107
Age	1.978	0.067	-0.29, 4.24	0.07	0.087
Gender	1.310	0.043	-0.98, 3.60	0.05	0.261
Joint, Knee	3.579	0.121	1.23, 5.92	0.12	0.003
Baseline wofu	0.255	0.303	0.19, 0.32	0.28	<0.001
Depress.	3.856	0.103	0.98, 6.73	0.11	0.009
Co-morbidity	0.842	0.114	0.28, 1.41	0.12	0.004

Adjusted R^2 = 0.13 (proportion of explained total variation by the model). Wofu = WOMAC function, Depress = depression, Co-morbidity = sum of co-morbid conditions, b = unstandardized beta coefficient, SE = standard error, CI = confidence interval.

Table 4-10 presents the coefficients of the final multiple regression model for the WOMAC function effect size. Thirteen variables were included in this model and only seven made it to the final model. The variables in the final model were DM status, age, gender, joint type, baseline WOMAC pain, baseline HUI3 pain and co-morbidity. The variables entered into the regression model with effect size as dependent variable accounted for about 30% of the explained variance in standardized change in function (effect size).

Diabetes status did not have a significant linear relationship with change in WOMAC function as represented by effect size in both univariate ($P > 0.05$, 95% CI = -0.14, 0.41) and multiple regression analyses ($P > 0.05$, 95% CI = -0.15, 0.32). The independent predictors for effect size were baseline WOMAC pain, HUI3 single attribute pain, gender, co-morbidity and type of joint operated. WOMAC pain at baseline was the most influential variable in predicting change in WOMAC function with standardized coefficient of 0.41.

The regression estimates for both six-month WOMAC and effect size models were checked for stability using the backward selection methods. The results for both forward and backward selection methods were similar showing stability of the regression parameter results.

Table 4-10: Multiple Linear Regression (Forward selection) for WOMAC Function Effect Size[a]

Variable	b	Standardized β	95% CI	Partial r	P
Intercept	-0.982				<0.001
Diabetes Status	0.085	0.025	-0.148, 0.318	0.029	0.474
Age	0.077	0.034	-0.077, 0.231	0.040	0.326
Gender	0.194	0.086	0.042, 0.346	0.101	0.013
Joint, Knee	0.417	0.187	0.262, 0.571	0.211	<0.001
Baseline wopa	-0.026	-0.409	-0.032, -0.021	-0.373	<0.001
Baseline SAU pain	0.275	0.081	0.004, 0.546	0.081	0.047
Co-morbidity	0.043	0.077	0.005, 0.081	0.089	0.028

Adjusted R^2 = 0.305 (proportion of explained total variation by the model). [a] Effect Size = difference between pre-operative and six-month WOMAC function, divided by the standard deviation of preoperative score, Wopa = WOMAC pain, SAU pain = Health Utility Index 3 Single Attribute pain, Co-morbidity = sum of co-morbid conditions. b = unstandardized beta coefficient, CI= confidence interval.

4.4.4 Regression Diagnostics

Table 4-11 presents the results of the regression diagnostics for the multiple regression models for the six-month WOMAC function and effect size. There was no collinearity among the independent variables in this study. The tolerance statistic was above 0.2 for all variables and the variance inflation factor was less than 10. The Durbin-Watson statistic was also within the suggested limit showing that the assumption of independence was met. The histograms and the plots of standardized residuals and standardized predicted value for the six-month

WOMAC and the effect size showed that assumptions of linearity, normality and equal variance were met (Figures 2, 3, 4 and 5 in Appendix 2).

Case-wise diagnostics showed that 31 and 26 cases of the total 613 in the multiple regression models respectively for the six-month WOMAC and the effect size had standardized residual outside the ± 2 standard deviations. These numbers were within the limit of 5% allowed outside the ± 2 standard deviations (which equals 31 cases of total 613 in the multiple regression models). Despite this finding, the cases outside ± 2 standard deviations were investigated further to see if they exerted undue influence on the regression models. The Cook's distance (Cook's di) was used to assess the influential effect of these cases. The Cook's di measures the influence of an observation and how much the regression coefficient changes when this particular observation was deleted. The Cook's di values for all cases for both final regression models were less than the recommended limit of di <1.

Table 4-11: Regression Diagnostic Statistics

	Six-month WOMAC Function		WOMAC Effect Size	
Durbin-Watson	2.024		2.003	
Cook's distance	0.002		0.002	
Variable	Tolerance	VIF	Tolerance	VIF
Diabetes status	0.97	1.04	0.97	1.04
Baseline WOMAC pain	NA	NA	0.67	1.50
Baseline WOMAC function	0.81	1.24	NA	NA
Baseline HUI3 SAU pain	NA	NA	0.68	1.46
Gender, male	0.95	1.05	0.96	1.04
Age	0.96	1.04	0.94	1.06
Co-morbidity	0.93	1.07	0.94	1.07
Depression present	0.93	1.08	NA	NA
Joint, knee	0.88	1.14	0.91	1.10

VIF = variance inflation factor, Effect size = difference between pre-operative and six-month WOMAC function, divided by the standard deviation of preoperative score, WOMAC = Western Ontario and McMaster Universities Osteoarthritis Index, HUI3 SAU pain= Health Utility Index 3 Single Attribute pain, Co-morbidity = sum of co-morbid conditions. NA = not applicable.

4.5 Surgical Information and Health Services Utilization

The majority of participants (all cases considered) received spinal anaethesia (NDM = 415, 66%; DM = 61, 74.4%). For THA, the preferred surgical approach was antero-lateral for both NDM (225, 78.7%) and DM (12, 57.1%). Most of the participants with THA had uncemented fixation method used (NDM = 206, 73.6%; DM = 16, 76.2%) - Table 4-1. There was no difference in the fixation method used for NDM and DM participants with THA (p = 0.79).

For participants with TKA, most had cemented fixation (NDM = 181, 54.4%; DM = 31, 52.5%) - Table 4-1. Similar to the participants with THA, there was no difference in the fixation method used for NDM and DM participants with TKA (p = 0.86). Most participants were discharged home with weight bearing as tolerated using a walking aid, 604 (95.9%) for NDM and 81 (98.8%) for DM participants (p = 0.15).

Most participants were discharged home, however, more NDM participants (388, 64.3%) were discharged home compared to DM (39, 52.0%) (p = 0.04). For TKA, 205 (61%) NDM and 28 (50.9) DM participants were discharged home (p = 0.16). Patients not discharged home were discharged to sub-acute, local hospitals or other locations. Among those discharged home, 238 (61.3%) and 145 (70.7%) of NDM participants (TJA and TKA respectively) received homecare or outpatient physiotherapy, while for DM participants (TJA and TKA respectively), 25 (64.1%) and 20 (71.4%) needed such services (p = 0.74 TJA and p = 0.94 for TKA). Despite no difference by DM status in the homecare or outpatient physiotherapy received, participants with DM discharged home had lower but non-significantly different six-month WOMAC function (DM = 23.5 (SD = 21.0), NDM = 16.9 (SD = 14.0), p = 0.07, 95% CI = -13.73, 0.53).

Most of the participants not discharged home lived alone ($p < 0.001$), were females (p = 0.03) and had lower six-month WOMAC function (p = 0.001, 95% CI = -6.84, -1.91) compared to those discharged home. And among those discharged home, participants with diabetes had lower insignificant function (p = 0.07, 95% CI = -13.73, 0.53).

Summary of findings

In summary, function as assessed by the WOMAC for the study participants was significantly better at six months post-operation compared to the pre-operation. There was a statistically significant difference in the six-month function scores between NDM and DM which, however, did not reach clinical significance.

All the independent variables considered in the multivariate analyses were similar for participants with NDM and DM, except for co-morbid conditions and BMI. Participants with DM had higher BMI scores and higher number of co-morbid conditions. Despite evidence of linear association between DM status and six-month function in univariate regression analyses, DM status was not a significant determinant of six-month WOMAC function and effect size in the multivariate analyses after controlling for the demographics, medical and clinical factors that could influence function.

CHAPTER FIVE

DISCUSSION

Functional outcomes after TJA in patients with diabetes have been given limited attention in the literature (Meding et al., 2003). No previous study has looked at function while controlling for diabetes and other factors that could influence function.

We found that previous attempts at evaluating function among patients with diabetes who underwent TJA mostly focused on clinical complications (rates of wound and joint infection, revision, and urinary tract infection), and survivorship analysis (England et al., 1990; Meding et al., 2003; Papagelopolous et al., 1996; Yang et al., 2001). These studies briefly reported on functional outcomes. The trend observed showed that patients with diabetes may have lower functional outcomes; but none of them statistically controlled for any other known prognostic factors that may influence function after TJA within diabetes patient populations (Meding et al., 2003; Papagelopolous et al., 1996).

Persons with DM in the general population have reduced function compared to those without DM (Gregg et al., 2000 & 2002). In studies involving the general population, significant association between DM and reduced function was maintained even after controlling for the other factors that could influence function (de Rekeneire et al., 2003). De Rekeneire and associates (2003) reported that the likelihood (odds) of having difficulty with up to three functional tasks reduced from 2.53 (95% CI = 1.69, 3.78) to 1.69 (95% CI = 1.10, 2.61) after adjusting for all relevant medical and clinical factors. Poor glycemic control contributed to the association between DM and lower function (de Rekeneire et al., 2003).

Hyperglycemia, which is an index of poor blood sugar control, has been linked with increased infection rates (Goodson & Hunt, 1979), and poor collagen formation and wound healing (Goodson & Hunt, 1978 & 1979; Lioupis, 2005). However, in the general population, not all patients with DM have as good control of blood sugar as seen in surgical patients. But it is not known whether good blood sugar control is enough to change how DM impacts on function (de Rekeneire et al., 2003).

The results of studies on the association between DM status and function in the general population are equivocal. There were debates on whether DM, independent of other co-morbid conditions, has a significant negative impact on function (de Rekeneire et al., 2003; Maddigan et al., 2005). There were no studies that have examined the effect of DM on function controlling for other covariates that could influence function in a cohort similar to that of this study. The lingering questions are whether DM would impact on function after TJA in a similar way as observed in the general population and if so, would this effect on function be explained on the basis of DM status alone, independent of other relevant factors that could influence function?

In an attempt to bridge some of the knowledge gaps in the literature, the present study therefore aimed at specifically evaluating the effect of diabetes status on function while controlling for covariates that may influence function and to compare function among patients with DM and NDM after TJA.

Effect of DM Status on Function

Unlike other studies, this study recorded a first in many areas. Notably, it was the first study to evaluate the effect of diabetes status on function after TJA while controlling for other covariates. Not only did we look at function at six months post-operatively, but also, we studied the effect size (standardized change in function).

Diabetes status had a linear relationship with the six-month WOMAC function at the univariate level, but lost the association at the multivariate level. Diabetes status did not have any linear relationship with the effect size of function at either the univariate or multivariate levels. These results suggest that DM status is not an independent predictor of function after TJA in this patient cohort. Therefore, DM status alone may not be a reason to expect poor functional outcomes after TJA. By the virtue of the significant linear relationship observed between DM status and six-month function at the univariate level, DM status is a factor that warrants further consideration.

Factors that were significantly associated with six-month function included baseline WOMAC function, co-morbidity, joint type, and depression.

And those factors that were significantly associated with the effect size are baseline WOMAC pain, HUI3 pain, co-morbidity, joint type, and gender.

The variables in the final models accounted for 13% and 30% of the explained variance seen in the six-month function and WOMAC effect size respectively. The explained variance for the six-month WOMAC function was slightly lower than that reported in other studies of the TJA population (Fortin et al., 1999; Jones et al., 2003; Sharma et al., 1996). It was not clear whether the explained variance seen within this study was related to this cohort. Due to small sample size for patients with DM who had THA, it was not possible to have separate models based on the types of joint operated. There were differences between the findings reported and earlier findings of other studies (Fortin et al., 1999; Jones et al., 2001). It was, however, difficult to say exactly what accounted for the low variance explained for the six-month function, given that we had also different independent variables included in our multivariate analysis. The explained variance for the effect size was comparable to that previously reported (Jones et al., 2001).

In the final multivariate model with the six-month WOMAC function as the dependent variable, baseline function was a strong independent predictor of six-month function. Comparable baseline function between patients with and without DM may explain the lack of clinically significant difference in function at six months. The importance of baseline function as a predictor of post-operative function has been reported widely in the TJA literature (Ethgen et al., 2004; Jones et al., 2003; Jones et al., 2005; Young et al., 1998).

Of note, there was no interaction effect on function between diabetes status and co-morbid conditions, in-hospital complications, body mass index, and baseline pain. Ordinarily, one would expect that the additive effects of these factors may have a larger impact on function, but this was contrary to our findings. The interaction term between diabetes and depression was significant at the bivariate level, but was not significant after controlling for independent variables such as baseline WOMAC function, co-morbidity, joint type and depression. Additive effects between interacting co-morbid conditions and diabetes in patients undergoing TJA resulted in a higher likelihood for non-homebound discharge in a previous study (Jain et al., 2005). Wee et al. (2005) and Maddigan et al. (2005) reported that the combination of diabetes with other co-morbid conditions (e.g. heart disease, stroke, arthritis etc) resulted in lower health related quality of life. These studies specifically combined diabetes with other chronic conditions, which was different from the intent of this study. A summary variable quantifying co-morbid conditions was used. The limitation of using a summative score to evaluate the effect of co-morbid conditions has been raised previously (Jones et al., 2005).

The number of co-morbid conditions significantly explained the six-month WOMAC function and the effect size. Greater number of co-morbid conditions in patients with DM has been associated with reduced function (Gregg et al., 2000; Maty et al., 2004; de Rekeneire et al., 2003). Similarly, increased co-morbid conditions have been reported in prospective cohort studies, in patients undergoing TJA to result in reduced function (Fortin et al., 1999 & 2002; Mahomed et al., 2002).

The importance of co-morbid conditions in explaining the burden of diabetes has been reported in an earlier study (Maddigan et al., 2005). The results of this study, particularly with regards to co-morbid conditions, were consistent with the conclusions drawn by Maddigan et al. (2005), that the burden of co-morbidity rather than DM status alone accounts for the reduced HRQOL seen in patients with DM. Co-morbidity was a significant determinant of six-month function and effect size while DM status was not. Diabetes should be considered as part of the patient's overall co-morbidity profile.

Post-operative complications have also been reported to be associated with a higher number of co-morbid conditions (Jain et al., 2005; Kreder et al., 2003). There was no significant difference between patients with and without diabetes regarding in-hospital complications in this study. Similar findings were reported by Meding et al. (2003). Conversely, Papagelopoulos et al. (1996) observed higher incidence of post-operative complications among patients with diabetes compared to matched controls. The differences in the follow-up periods (52 to 96 months) may make it difficult to directly compare the results of this study with those of the previous studies. However, it is possible that peri-operative and post-operative care continues to improve with time; thus DM management for surgical patients may also be improving thereby reducing post-operative complications.

In-hospital complications did not contribute significantly to explaining six-month function and change in function at the multivariate level. Participants with diabetes in this cohort seemed healthier when characteristics at baseline were compared to NDM participants; which may partly explain the non-significant findings. This in turn may be explained in two ways; firstly, there may be preferential bias in the referral and selection of candidates for surgery (Hawker et al., 2000; Skinner et al., 2003). Secondly, the management of patients with diabetes undergoing surgery to increase safety and prevent complications includes tight blood sugar control (Jacober & Sowers, 1999).

Depression was a significant determinant of the six-month WOMAC function. Previous studies have reported increased likelihood of functional disability in patients with depression (Black et al., 2003; Egede, 2004). Presence of both DM and depression increased the likelihood of functional disability even further (Black et al., 2003; Egede, 2004). The prevalence of functional disability was as high as 78% in the presence of both DM and depression compared to just 25% in people without both conditions (Egede, 2004).There was a trend towards a significant additive effect of DM and depression on the six-month function at the interaction model building stage in our analyses. Our results did not show that a combination of DM and depression significantly explained the six-month function after controlling for other demographics, medical and clinical factors. Brander et al. (2003) reported the presence of significantly more pain in patients with TKA who had pre-operative depressive symptoms. This may partly explain the association between depression and function given the high correlation between WOMAC pain and function ($r = 0.74$) in our study.

Previous studies have reported a significant association between diabetes and higher BMI scores, which are consistent with the findings of this study (Jibodh et al., 2004; Mokdad et al., 2003; Namba et al., 2005). Likewise, patients undergoing TJA have significantly higher rates of obesity compared to the general population, with a stronger trend among patients having TKA than THA (CJRR, 2005, Namba et al., 2005). Previous studies on the effect of obesity on functional outcomes have been equivocal. The inconsistency in findings was attributed to many factors including the differences in the follow-up periods, definition of obesity, and inability to fully assess the influence of other co-morbid conditions (Jibodh et al., 2004; Moran et al., 2005). While comparable early functional outcomes have been reported between patients with and without obesity by some authors (Deshmukh et al., 2002; Jibodh et al., 2004; Moran et al., 2005), others have found worse functional status among patients with obesity after THA (Bischoff-Ferrari et al., 2004). The results of this study did not show that BMI has an independent relationship with function after controlling for the other variables.

Function in patients with and without diabetes

All participants in this study showed clinically significant improvement in function at six months post-operation and the change in function (effect size) similarly improved. Comparison of the results of this study to others that used WOMAC function showed that patients irrespective of joint replaced do have marked improvement in physical function after TJA (Bachmeier et al., 2001; Fortin et al., 1999; Jones et al., 2001 & 2003; Nilsdotter et al., 2003). The change in function for patients without DM observed in this study was similar to that reported by Fortin et al. (1999), and Jones et al. (2001 & 2003). Fortin et al. (1999) divided their sample into low and high functioning groups based on the pre-operative function score. The low functioning group had change in function similar to the results reported by this study, and coincidentally, most of the patients in this group were recruited from the Canadian population (as opposed to the high functioning group which were mostly USA residents).

The majority of patients in this study had a 10-point change in function (the minimum clinically important difference) at six months. Analysis of the results based on joint types showed that the percentage that did not show a 10-unit change in function was similar to those of Jones et al. (2003) and Nilsdotter et al. (2003). The differences in the results of these two previous studies generally reflected the fact that THAs show better functional outcomes than TKAs. It is interesting that the findings of this study were consistent with that of Nilsdotter et al. (2003) despite their longer follow-up period of 3.6 years. However, some authors have reported that most improvement occurs in the first three to six months post-operatively (Fitzgerald et al., 2004), which may explain the similarity in the findings irrespective of the differences in the follow-up periods between this study and that of Nilsdotter et al. (2003).

Participants with DM enjoyed benefits of TJA as seen in the significant improvement in function score from baseline to six months post-operation as indicated above. The findings of this study are similar to those of previous studies that have reported significant improvement in function in patients with DM after

TJA (Meding et al., 2003; Papagelopoulos et al., 1996; Serna et al., 1994; Yang et al., 2001).

Serna et al. (1994) in a retrospective review showed that patients with DM improved on the Hospital for Special Surgery (HSS) Scale from a pre-operative score of 50 to 85 post-operatively. Similarly, Meding et al. (2003), Papagelopoulos et al. (1996) and Yang et al. (2001) reported statistically higher post-operative Knee Society (KS) rating scores in patients with DM they studied. Direct comparison of our results with previous studies is difficult because the follow-up period (52 to 96 months) and outcome measures used to evaluate function differ. Function in the earlier studies was evaluated by clinically-based tools (e.g. the Knee Society Rating Scale) while this study used a self- reported function.

Comparison of functional outcomes between patients with and without diabetes showed that there was no significant clinical difference in the six-month function and the effect size between the two groups. But the level of function at six months (the six-month WOMAC function) was significantly lower statistically for patients with diabetes. The finding of statistically lower function for patients with DM was consistent with previous studies comparing patients with DM and NDM except that the average follow-up periods (i.e. 53 months) were strikingly longer than for this study (Meding et al., 2003; Serna et al., 1994). Serna et al. (1994) reported statistically significant difference between patients with DM and NDM using the Hospital for Special Surgery (HSS) and the KS rating scales. The HSS average scores reported for patients with DM and NDM post-operatively were 85 (43 knees were rated excellent or good on the KS rating scale) and 92 (51 were rated excellent or good on the KS rating scale).

Despite the long follow-up period, Meding et al. (2003) in their study evaluated function periodically starting from six months post-operatively; therefore part of their results are comparable with those of this study. Patients with DM had statistically lower Knee Society function pre-operatively and at all post-operative periods. Participants with and without DM had statistically similar baseline functions, but had a significant difference in function at six months, in our cohort. The difference between patients with and without DM was not clinically significant at six months post-operative period as defined by a 10-point change in WOMAC function. Lack of clinically significant difference in function may be due to the atypical similarities at baseline for participants with and without DM. This limits generalization of our results to the larger DM population who typically have lower function (de Rekenere et al., 2003; Gregg et al., 2000 & 2002; Meding et al., 2003).

Lack of a clinically important difference in function at six months between patients with and without diabetes further reinforce the fact that DM status may not affect function after TJA. The statistically significant difference in the six-month WOMAC function may be related to our large sample size and some differences in baseline characteristics for patient groups with DM and NDM in our cohort. Patients with DM had a higher number of co-morbid conditions, which significantly explained the six-month function in the multivariate analysis.

The change in function score and the effect size were comparable for patients with and without diabetes after TJA. The previous studies that have examined functional outcomes after TJA between patients with DM and NDM looked at the level of function at various post-operative periods and did not focus on change in function (Meding et al., 2003; Serna et al., 1994). These studies found a lower level of function in patients with diabetes, but in one study that provided the pre-operative score, these patients started with a lower level of function even before their operation (Meding et al., 2003). It follows that patients with DM may be functioning at levels below their NDM counterparts pre- and post-operatively, but the magnitude of change in function seen in patients with DM are comparable to the NDM. Therefore, patients with diabetes have potential to show improvement comparable to NDM patients.

More patients with diabetes than without were not discharged home. This difference may be due in part to a combination of factors including in-hospital complications, co-morbid conditions, level of function, and social support. Patients with diabetes had a significantly higher number of co-morbid conditions, and specifically a higher number of patients with DM had hypertension and kidney disease. Patients not discharged home also likely lived alone, was a female and had lower six-month function. It was not the intention of this study to examine how factors above interact but previous studies have reported that older age, female gender, living alone, lower function, obesity, diabetes and increased co-morbid conditions are factors related to the need for admission to a rehabilitation unit (De Pablo et al., 2004; Forrest et al., 1998; Munin et al., 1995; Jones et al., 2001; Jones et al., 2003).

Among those discharged home, there was no difference in the homecare support and outpatient physiotherapy services received. The specifics of the type of physiotherapy received could not be ascertained by this study. Among those who were discharged home, DM participants had lower six-month WOMAC function than NDM, with a trend towards significance. Since patients improved as the post-operative period progressed, the difference could have been greater earlier in the post-operative period. Further investigation of the healthcare service support received in the period up to the six months may be warranted.

Limitations

There are some limitations to this study. Diabetes is considered a heterogenous disease with varying severity, a fact which must be considered when comparing patient outcomes (Meding et al., 2003). The inability to differentiate the types of diabetes or collect information regarding duration of diabetes and the level of glycemic control may be a limitation of this study. The participants with diabetes in this cohort seemed healthier considering the comparable characteristics at baseline with the NDM participants. This may be related to the preferential referral and selection biases seen among people who were to receive TJA and the practice of tightening blood glucose control prior to surgery to prevent complications (Jacober & Sowers, 1999).

Bachmeier et al. (2001) reported up to 25% difference in improvement in physical function between patients after THA and TKA, with those who had THA having higher function. Despite reported differences in functional outcomes for THA and TKA, separate models for THA for the regression analysis could not be done because of small sample size of patients with DM with THA. It is not known whether the results based on joint types would be similar to our results.

The follow-up period was only for six months. Though relatively short, this seemed appropriate considering the fact that most of the complications that could influence recovery occur in the early post-operative period among patients with DM (Meding et al., 2003). Also, most patients after TJA show improvement even as early as three months post-operation (Fitzgerald et al., 2004; Laupacis et al., 2002), with the greatest change in function occurring in the first three to six months (Bachmeier et al., 2001).

Similarity in the baseline function of patients with and without DM limits generalization of our results to the larger population of patients with DM. Typically, patients with DM have been reported to function below their NDM counterparts (Gregg et al., 2000 & 2002; Meding et al., 2003). The elective nature of TJA procedure for participants in this cohort and the selection bias by surgeon could be contributing factors (Hawker et al., 2000).

This study did not have community rehabilitation data. There may have been some differences in the details of rehabilitation received after discharge from the hospital. However, rehabilitation received after discharge from the hospital was based on individual patient's need. No clinically significant differences were seen in function at six months which probably indicates that patients' rehabilitation needs were met.

The discrepancies between self-report and performance based functional measures have been raised as a limitation especially during periods when functional status may be changing (Jones et al., 2003). However, assessment of function during relatively stable periods (about a month before surgery and at six months post-operatively) may provide valid self-reported assessment of function (Jones et al., 2003). Self-reported function as used in this study may have an edge because it tends to reflect patient's own estimate of ability and as such it is devoid of observer bias (Lingard et al., 2001). This is the first study to use WOMAC function among patients with diabetes who received TJA.

In conclusion, despite the limitations, the findings from this study provided evidence that DM status may not be a reason for reduced function after TJA. The importance of baseline function as a key determinant of post-operative function was reiterated. And with good baseline function, patients with DM could achieve comparable level of function as their NDM counterparts.

CHAPTER SIX

SUMMARY AND CONCLUSIONS

6.1 SUMMARY AND CONCLUSIONS

Based on the results of this study, the following conclusions can be made:

1. Diabetes status did not negatively impact the six-month WOMAC function and change in function (effect size) after controlling for demographics, medical and clinical factors that could influence function.
2. Participants with and without DM had significant improvement in function at six months after TJA. There was no clinically significant difference in the six-month WOMAC function between participants with and without diabetes. But the baseline function levels also were similar for patients with and without DM. Effect size for WOMAC function was also not different between participants with and without diabetes.

6.2 CLINICAL IMPLICATIONS

Diabetes, a multi-system disorder, is associated with both reduced subjective and objective function (Gregg et al., 2000 & 2002). There is also a higher number of co-morbid conditions associated with DM which could influence function. Accounting for the presence of co-morbidities attenuates

DM's association with reduced function, but a significant association persisted as reported in previous studies in the general population (Gregg et al., 2000; de Rekeneire et al., 2003). An independent contribution of DM to functional deficits therefore exists in the general DM population. Dysfunction is one of the clinical problems of patients after TJA. The relationship between DM status and function has not been clearly elucidated in people undergoing TJA.

This study did not provide evidence to support the presence of an independent relationship between DM and function after controlling for relevant demographics, medical and clinical factors. Factors that were statistical determinants of the six-month function included baseline WOMAC function, co-morbidity, joint type, and depression.

Participants with and without DM had clinically comparable function at six months post-operatively but had similar baseline function too. Despite these findings, there is an indication that DM may still be a factor to consider in rehabilitation plans post TJA. This is because participants with DM had lower statistically significant function at six months post-operatively and DM had a significant linear relationship at the univariate level with six-month function. Difference in function at six months could be higher if the baseline function had not been similar between DM and NDM. Diabetes should be considered as part of the patient's overall co-morbidity profile. Comparable change in function between DM and NDM could be interpreted to mean that DM participants had potential to improve in function in a way similar to NDM.

Our findings may not generalize to the DM population receiving TJA. There are at least two reasons; first, the number of patients with DM who had THA in this study was small. This small sample of patients with DM who had THA prevented us from being able to have separate regression models for THA. Therefore, our results for TJA ignored the established functional differences that exist between patients who had THA and TKA. Secondly, patients with DM in our cohort functioned at a higher level comparable to those without DM, which was atypical for patients with DM.

6.3 FUTURE RESEARCH

Some suggestions for future research would be:

1. To investigate the effect of DM on function with a larger sample of patients with diabetes than was available for this study with the possibility of analyzing the TJA data separately for joint types and differentiating the effects of types of DM on function after TJA. This could be done through a case-control design or a prospective multi-centre study which would involve more patients.
2. To investigate the effect of rehabilitation received on functional outcomes for patients with DM during the early post-operative period.

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APPENDIX 1

Sample size calculations

Sample size for multiple regression analysis

The independent variables that were used as correlates of post-operative function are the demographic variables (age, gender, and level of education), the medical variables (Diabetes status, BMI, number of co-morbidities, depression, type of joint operation, pre-operative WOMAC joint function, WOMAC joint pain and HUI3 single attribute pain) and the peri-operative variable (number of in-hospital complications).

Power Analysis and Sample Size (PASS ® 2000) statistical program was used in calculating the sample size (Hintze, 2000). Sample size (n) is calculated from the non-centrality parameter λ, given as:

$\lambda = u\,(F_{u,v})$ where u is a constant, and $F_{u,v}$ has u numerator degree of freedom and v denominator degrees of freedom. The formula for $F_{u,v}$ incorporates the effect size, f^2 (Cohen, 1988).

$f^2 = \quad R^2_{TIC} / (1 - R^2_C - R^2_{TIC})$

$F = f^2 / v$

$F = (R^2_{TIC} / u) / (1 - R^2_C - R^2_{TIC})) / v \qquad v = N-K-1$

$R^2_{TIC} = R^2$ change when the variable of interest is added to the model

$R^2_C = R^2$ of the model with only the control variables

C = control variables, T = variable (s) of interest n = total sample size, U = number of variables, K = total number of all variables

$R^2_{TIC} = R^2_{TC} - R^2_C$ and R^2_{TC} = coefficient for the full model with all the variables.

For the calculation of sample size (N) using PASS Program, the following parameters were used:

T = variable(s) of interest = DM status, C = control variables = Eleven covariates

R^2 change when the variable of interest (DM status) is added to the model containing covariates = 0.02

R^2 when the control variables are in the model = 0.20 to 0.30

$\alpha = 0.05$ $\beta = 0.20$

The sample size is as indicated below for the corresponding total R^2 with R^2 change hypothesized to be 0.02:

Total variance	**Sample size**
0.20	309
0.21	305
0.22	301
0.23	297
0.24	293
0.25	289
0.26	285
0.27	281
0.28	277
0.29	273
0.30	269

For a conservative total R-square of 0.20 and R^2 change of 0.02 when DM status is added to the model already containing the other covariates, a sample size of 309 was required.

Using the principle on which the PASS program was based on, the computation of the approximate sample size needed for the multiple regression is shown below (Maxwell, 2000):

$n = \lambda \left((1-R^2) \div R^2_C \right) + P-1$

λ = non-centrality parameter λ is a constant, and for $\beta = 0.20$ is given as 7.85.

$R^2 = R^2$ when the control variables are in the model = 0.20

$R^2_C = R^2$ change when the variable of interest (DM status) is added to the model containing covariates = 0.02

P = number of independent variables in the model

$n = 7.85 \left((1-0.20) \div 0.02 \right) + 12-1$

$n = (6.28 \div 0.02) + 11 = 325.$

Sample size for the Student t-tests

Estimating using data from Jones et al (2001), with a population similar to that used in this study, the standard deviation was 17 and the minimal significant change was 10. The z value for $\alpha = 0.05$ for a two-tailed test and power of 80% ($\beta = 1 - 0.8 = 0.20$) are 1.96 and 0.84 respectively. The formula for sample size calculation for two means is given as below (Angst, Aeschlimann, & Stucki, 2001; Norman and Streiner, 2000):

$n = 2 (Z_1 + Z_2)^2 \sigma^2 / d^2$

n = sample size

Z = z-value at $\alpha = 0.05 = 1.96$ and $\beta = 0.20 = 0.84$

σ = standard deviation, d = change score = minimum detectable change

$= 2\ (1.96 + 0.84)^2\ 17^2 / 10^2 = 2\ (7.84 \times 289) / 100 = 4531.52 / 100 = 45.32$

n = approximately 46 per group.

Note: very similarly, using effect size (Cohen, 1988) of 0.6 (moderate effect size) instead of the standard deviation and the minimum detectable change yielded sample size of 44.

APPENDIX 2

Tables and figures for additional results

Table 1- The completion rates for the WOMAC subscales pre-operatively and six-month follow-ups

WOMAC n= 715	Valid questions	Missing ≥2 or 4	Missing ≤1 or 3	Completely missing	Total missing
Baseline pain	5	4	0	6	10
Baseline stiffness	2	0	0	6	6
Baseline function	17	4	0	5	9
six-month function	17	2	0	76	78

Table 2: Comparison of participant and non-participant characteristics

	Participants			Non-participants		
Joint type	TJA	THA	TKA	TJA	THA	TKA
Age, mean (SD)	66.8 (10.4)	65.7 (10.4)	67.6 (10.4)	69.0 (10.8)	67.8 (11.6)	70.2 (10.0)
Gender, Female n (%)	430 (60.1)	179 (58.3)	251 (61.5)	96 (56.5)	41 (52.6)	55 (59.8)
P-value		0.39			0.34	
Side operated, Left n (%)	327 (45.7)	138 (45.0)	189 (46.3)	70 (41.2)	32 (51.6)	38 (50.7)
P-value		0.72			0.91	

Figure 1: Study participants' flowchart for the primary analysis using WOMAC function subscale

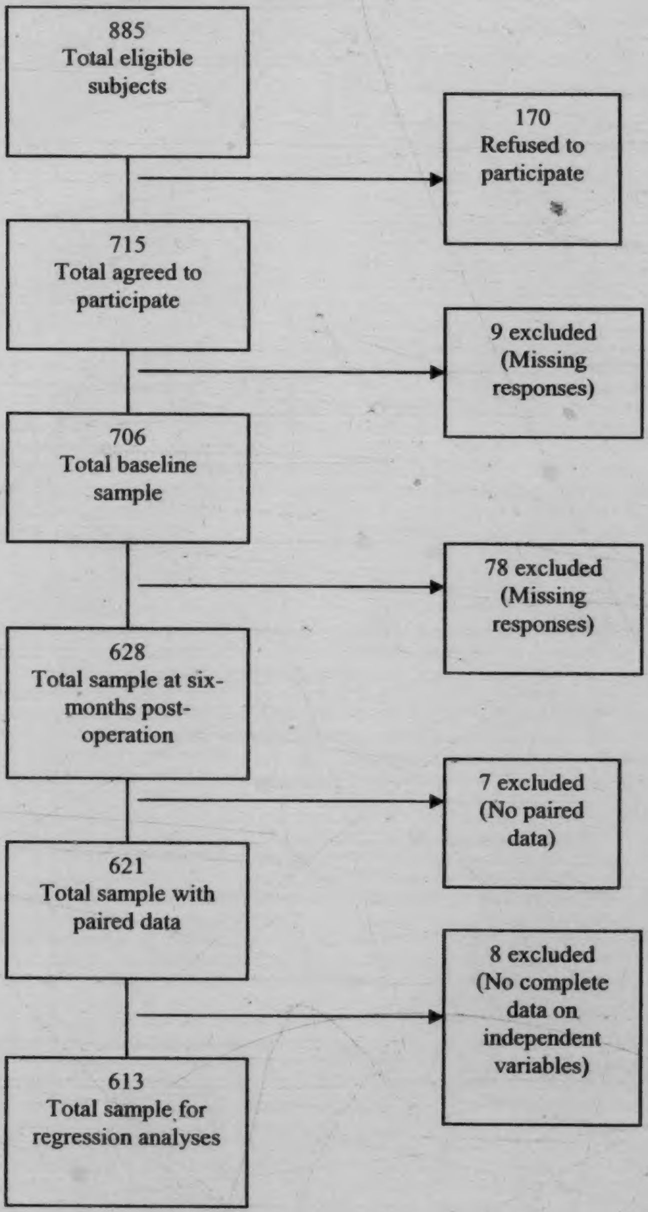

885
Total eligible subjects
170
Refused to participate
715
Total agreed to participate
9 excluded
(Missing responses)
706
Total baseline sample
78 excluded
(Missing responses)
628
Total sample at six-months post-operation
7 excluded
(No paired data)
621
Total sample with paired data
8 excluded
(No complete data on independent variables)
613
Total sample for regression analyses

Table 3: Number (%) of participants reporting moderate to extreme difficulty on the WOMAC function questions pre-operatively

	TJA		TKA	
WOMAC questions	NDM n (%)	DM n (%)	NDM n (%)	DM n (%)
Descending stairs	513 (81.9)	68 (82.9)	286 (83.6)	51 (83.6)
Ascending stairs	531 (85.0)	69 (84.1)	284 (83.3)	50 (82.0)
Rising from sitting	485 (77.4)	63 (76.8)	253 (74.0)	45 (73.8)
Standing	447 (71.2)	66 (80.5)	235 (68.5)	48 (78.7)
Bending to the floor	450 (72.0)	64 (78.0)	216 (63.3)	44 (72.1)
Walking on a flat surface	454 (72.6)	60 (73.2)	223 (65.4)	43 (70.5)
Getting in/out of car	494 (78.7)	62 (75.6)	244 (71.1)	42 (68.9)
Going shopping	510 (81.5)	67 (81.7)	266 (77.8)	49 (80.3)
Putting on stockings	399 (63.6)	48 (58.5)	164 (48.0)	28 (45.9)
Rising from the bed	401 (63.9)	49 (59.8)	185 (53.9)	31 (50.8)
Taking off stockings	357 (57.0)	42 (51.2)	140 (41.1)	25 (41.0)
Lying in bed	303 (48.4)	39 (47.6)	120 (35.2)	23 (37.7)
Getting in out of bath	400 (63.8)	58 (70.7)	203 (59.2)	39 (63.9)
Sitting	291 (46.4)	37 (45.1)	124 (36.2)	23 (37.7)
Getting in/off toilet	362 (57.7)	50 (61.0)	161 (47.1)	32 (52.5)
Heavy domestic duties	528 (84.5)	71 (86.6)	284 (83.3)	53 (86.9)
Light domestic duties	348 (55.7)	51 (62.2)	160 (46.9)	37 (60.7)

Table 4: Number (%) of participants reporting moderate to extreme difficulty on the six-month WOMAC function questions

	TJA		TKA	
WOMAC questions	NDM n (%)	DM n (%)	NDM n (%)	DM n (%)
Descending stairs	127 (22.8)	23 (31.9)	100 (33.3)	20 (38.5)
Ascending stairs	115 (20.6)	20 (27.8)	73 (24.3)	16 (30.8)
Rising from sitting	115 (20.6)	26 (36.1)	78 (26.0)	22 (42.3)
Standing	83 (14.9)	15 (20.8)	57 (19.0)	13 (25.0)
Bending to the floor	211 (37.8)	33 (45.8)	81 (26.9)	20 (38.5)
Walking on a flat surface	43 (7.7)	9 (12.5)	28 (9.3)	8 (15.4)
Getting in/out of car	128 (22.9)	25 (34.7)	77 (25.6)	20 (38.5)
Going shopping	111 (19.9)	23 (31.9)	70 (23.3)	20 (38.5)
Putting on stockings	122 (21.9)	17 (23.6)	46 (15.3)	11 (21.2)
Rising from the bed	47 (8.4)	11 (15.3)	32 (10.7)	9 (17.3)
Taking off stockings	71 (12.7)	11 (15.3)	28 (9.3)	8 (15.4)
Lying in bed	31 (5.6)	8 (11.1)	22 (7.3)	8 (15.4)
Getting in out of bath	93 (16.7)	22 (30.6)	53 (17.7)	17 (32.7)
Sitting	31 (5.6)	8 (11.1)	21 (7.0)	8 (15.4)
Getting in/off toilet	43 (7.7)	16 (22.2)	31 (10.4)	12 (23.1)
Heavy domestic duties	350 (62.9)	46 (63.9)	186 (62.2)	31 (59.6)
Light domestic duties	79 (14.2)	15 (20.8)	43 (14.4)	8 (15.4)

Table 5: Number (%) reporting presence of co-morbid conditions on Charlson Index by diabetes status

	TJA		TKA	
Co-morbid conditions	NDM	DM	NDM	DM
Chronic back pain	222 (35.1)	32 (39.0)	131 (37.8)	24 (39.3)
Serious problem with joint or bone	55 (8.7)	7 (8.5)	31 (8.9)	5 (8.2)
Circulatory*	82 (13.0)	16 (19.5)	47 (13.5)	12 (19.7)
High blood pressure	279 (44.1)	57 (69.5)	174 (50.1)	42 (68.9)
Heart disease*	133 (21.0)	21 (25.6)	76 (21.9)	14 (23.0)
Emphysema/bronchitis	58 (9.2)	5 (6.1)	26 (7.5)	5 (8.2)
Asthma	57 (9.2)	7 (8.5)	31 (8.9)	6 (9.8)
Cancer	63 (10.0)	10 (12.2)	27 (7.8)	4 (6.6)
Digestive problems	124 (19.6)	7 (8.5)	75 (21.6)	5 (8.2)
Stomach ulcer	38 (6.0)	2 (2.4)	26 (7.5)	2 (3.3)
Goiter or thyroid	96 (15.2)	9 (11.0)	54 (15.6)	8 (13.1)
Kidney*	20 (3.2)	7 (8.5)	12 (3.5)	4 (6.6)
Liver disease	8 (1.3)	1 (1.2)	5 (1.4)	1 (1.6)
Eyes problems*	193 (30.5)	29 (35.4)	120 (34.6)	19 (31.1)
Epilepsy	4 (0.6)	0 (0.0)	2 (0.6)	0 (0.0)
Paralysis/speech problems due to stroke	6 (0.9)	3 (3.7)	4 (1.2)	2 (3.3)
Long term conditions e.g. post-polio, MS, Parkinson, others	55 (8.7)	12 (14.6)	30 (8.6)	10 (16.4)

* For these conditions data from chart review and self report were combined.

Table 6: Pearson correlation coefficients for continuous independent variables

	WOMAC pain	HUI3 pain	WOMAC function	Age	BMI
WOMAC pain		-0.55	0.74	-0.18	0.09
HUI3 pain			-0.54	0.14	-0.12
WOMAC function				-0.11	0.06
Age					-0.19

Table 7: Multiple Linear Regression (Forward selection) for Six-month WOMAC Function (using top six co-morbid conditions and three in-hospital complications)

Variable	b	Standard-Ized β	95% CI	Partial r	P
Intercept	0.567				0.808
Diabetes Status	3.074	0.067	-0.40, 6.55	0.07	0.083
Age	2.478	0.083	0.23, 4.72	0.09	0.031
Gender	1.120	0.037	-0.17, 3.41	0.04	0.337
Joint, Knee	3.767	0.127	1.42, 6.11	0.13	0.002
Baseline wofu	0.255	0.303	0.19, 0.33	0.28	<0.001
Depress.	4.110	0.110	1.24, 6.98	0.11	0.005
Chronic LBP	2.433	0.080	0.10, 4.77	0.08	0.041

Adjusted R^2 = 0.124 (proportion of explained total variation by the model). wofu = baseline WOMAC function, Depress = depression, LBP = low back pain, b = unstandardized beta coefficient, SE = standard error, CI = confidence interval.

Figure 2: Scatter plot for standardized residual and standardized predicted value for six-month WOMAC function

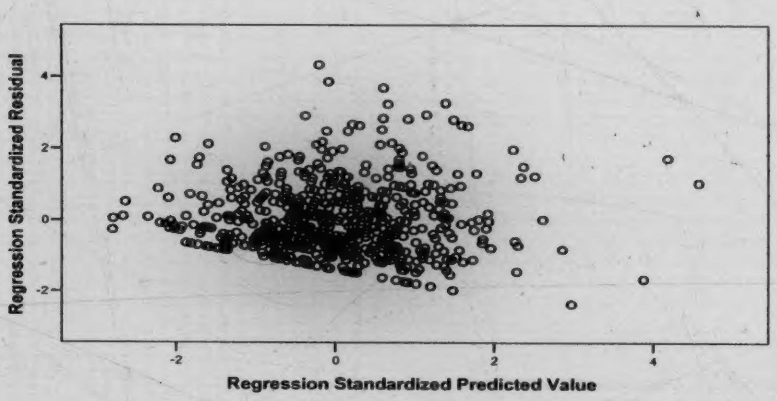


Figure 3: Histogram for the six-month WOMAC function

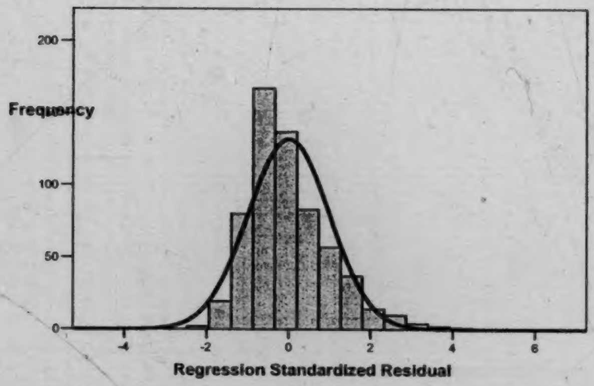


Figure 4: Scatter Plot for Standardized Residual and Standardized Predicted Value for Effect size WOMAC Function

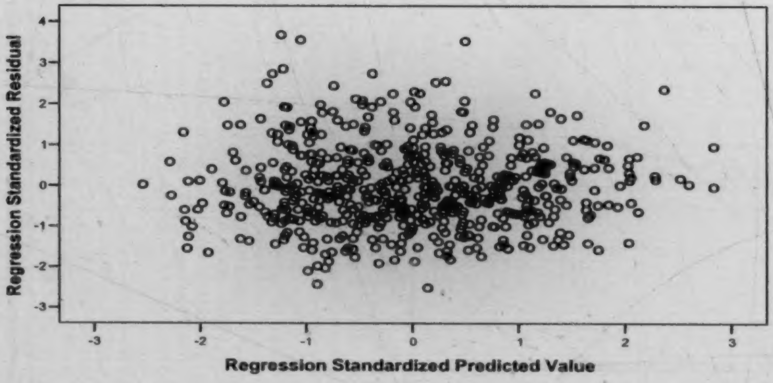
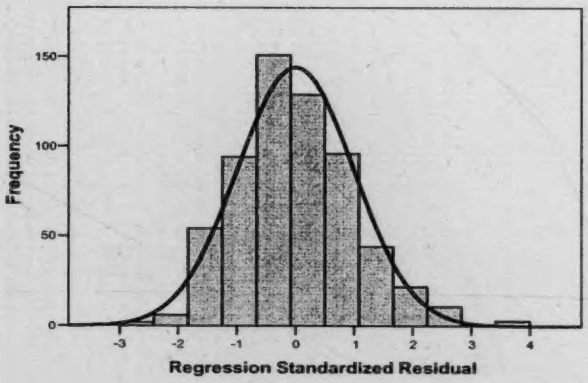


Figure 5: Histogram for the WOMAC effect Size



APPENDIX 3

Forms for data collection

STUDY QUESTIONNAIRES: BASELINE DEMOGRAPHIC: JOINT REPLACEMENT

0 RAH 1 UAH 2 MIS INTERVIEWER ______________________

Please insert
patient ID
sticker here

Date: (dd/mmmm/yy)__________________________

Joint ☐0 Hip ☐1 Knee

Side ☐0 Left ☐1 Right

WELLNET on chart ☐ 1 Yes
☐ 0 No, please ask ward clerk to print WELLNET

Address: ____ City/town:

Postal Code: __________________ Telephone Number:

Family Doctor__________________________

CONTACT PERSON:(does not live with person):(relationship) __________________________

City:____ (Phone)__________________

Marital Status: ☐ 1 Married/common-law ☐2 Single/Never married ☐ 3 Widowed
☐ 4 Separated ☐ 5 Divorced

Gender: ☐ 0 Female ☐ 1 Male

Date of Pre-Admission (dd/mmm/yy) ______________________

Date of Surgery (dd/mmm/yy)______________________

Will this patient be able to converse over the telephone for the follow-up? ☐1. Yes ☐0. No
If no, why? ____

Distance Walked:	Support:	How many stairs can you climb? (1 flight = 13 stairs)
☐0 unlimited (10 blocks or >)	☐0 None	
☐1 6 – 10 blocks	☐1 1 cane	
☐2 1 – 5 blocks	☐2 1 crutch	
☐3 < 1 block	☐3 2 canes	
☐4 indoors only	☐4 2 crutches	
☐5 unable to walk	☐5 walker	
	☐6 wheelchair	

What factor limits your walking?
☐0 no limit ☐ 1 pain/discomfort ☐2 fatigue ☐3 other ______________

LEVEL OF DISABILITY - OTHER JOINTS:

	None	Mild	Moderate	Severe	Replaced	Fused
IPSILATERAL: L R						

Hip	☐	☐	☐	☐	☐S / AS	☐
Knee	☐	☐	☐	☐	☐S / AS	☐
Ankle	☐	☐	☐	☐	☐S / AS	☐
Upper Extremity	☐	☐	☐	☐	☐S / AS	☐

CONTRALATERAL: L R	None	Mild	Moderate	Severe	Replaced	Fused
Hip	☐	☐	☐	☐	☐ S / A	☐
Knee	☐	☐	☐	☐	☐ S / AS	☐
Ankle	☐	☐	☐	☐	☐ S / AS	☐
Upper Extremity	☐	☐	☐	☐	☐S / AS	☐

Who lives with you (check as many as apply)

☐1. Home alone ☐2. Husband or wife ☐3. Children
☐4. Brothers and sisters ☐5. Grandchildren ☐6. Friends
☐7. Other relatives (does not include in-laws covered in the above categories)
☐8. Non-related paid helper (includes free-room)
☐9. Home unspecified ☐10. Seniors Home/Apt ☐11. Nursing home/Auxiliary
☐12. Other (specify):______________________________

What is your highest level of education completed?

☐1. No Schooling
☐2. Elementary grade_______
☐3. Junior High grade_______
☐4. High School grade_______
☐5. Non-University Degree (Vocational, Technical, Nursing)________________

University

☐6. partial
☐7. undergraduate degree
☐8. graduate degree

What is your employment status?

☐1. Employed full time
☐2. Employed part time
☐3. Unemployed
☐4. Retired
☐5. Student
☐6. Disability

Co-morbid Conditions

I would like to ask you about certain chronic health conditions, which you may have. We are interested in "long-term physical an d mental conditions" that have lasted or are expected to last 6 months or more.

Please tick the following conditions that apply to you.

Over the past week how much of a problem have the following conditions been to you when performing your regular activities

Present		None	Mild	Moderate	Severe	Do not know
☐	**Chronic pain:**					
	☐ back	☐	☐	☐	☐	☐
	☐ neck	☐	☐	☐	☐	☐
	☐ migraine	☐	☐	☐	☐	☐
	☐ abdomen	☐	☐	☐	☐	☐
	☐ chest	☐	☐	☐	☐	☐
	☐ other ____________	☐	☐	☐	☐	☐
☐	Serious problems with joints or bones (ie Paget's)	☐	☐	☐	☐	☐
☐	Osteoporosis	☐	☐	☐	☐	☐
☐	Arthritis/rheumatism: type ________	☐	☐	☐	☐	☐
☐	Circulatory Problems	☐	☐	☐	☐	☐
☐	High blood pressure	☐	☐	☐	☐	☐
☐	Heart disease	☐	☐	☐	☐	☐
☐	Emphysema/bronchitis/persistent cough	☐	☐	☐	☐	☐
☐	Asthma	☐	☐	☐	☐	☐
☐	Cancer: type: _________________	☐	☐	☐	☐	☐
☐	Digestive problems	☐	☐	☐	☐	☐
☐	Stomach ulcer	☐	☐	☐	☐	☐
☐	Diabetes	☐	☐	☐	☐	☐
☐	Severe Diabetes (with organ involvement)	☐	☐	☐	☐	☐
☐	Goiter or thyroid trouble	☐	☐	☐	☐	☐
☐	Kidney disease	☐	☐	☐	☐	☐
☐	Liver disease	☐	☐	☐	☐	☐
☐	Moderate/severe liver disease (cirrhosis)	☐	☐	☐	☐	☐

Present		None	Mild	Moderate	Severe	Do not know
☐	Allergies:					
	☐ Skin	☐	☐	☐	☐	☐
	☐ Food	☐	☐	☐	☐	☐
	☐ Hay fever or other allergies	☐	☐	☐	☐	☐
☐	Eye problems	☐	☐	☐	☐	☐
☐	Trouble hearing/deafness	☐	☐	☐	☐	☐
☐	Epilepsy	☐	☐	☐	☐	☐
☐	Paralysis/speech problems due to stroke	☐	☐	☐	☐	☐
☐	Sinusitis	☐	☐	☐	☐	☐
☐	Urinary incontinence	☐	☐	☐	☐	☐
☐	Alzheimer's disease/dementia	☐	☐	☐	☐	☐
☐	Mental problems					
	☐ depression	☐	☐	☐	☐	☐
	☐ anxiety	☐	☐	☐	☐	☐
	☐ panic	☐	☐	☐	☐	☐
	☐ other ________________	☐	☐	☐	☐	☐
☐	Long term conditions:					
	☐ Post polio syndrome	☐	☐	☐	☐	☐
	☐ Multiple sclerosis	☐	☐	☐	☐	☐
	☐ Parkinsons	☐	☐	☐	☐	☐
	☐ Other ________________	☐	☐	☐	☐	☐

MEDICATIONS

In the past month, did you take any of the following medications?

☐ No Medication:

	Yes	No	Don't Know
[illegible]			
Tranquilizers such as valium	☐	☐	☐
[illegible]			
Anti-depressants	☐	☐	☐
[illegible]			
Allergy medicine such as Sinutab	☐	☐	☐
[illegible]			
Cough or cold remedies	☐	☐	☐
Penicillin [illegible]			
Medicine for the heart (excluding medications for high cholesterol)	☐	☐	☐
Medicine for blood pressure			
Diuretics or water pills	☐	☐	☐
Steroids			
Insulin	☐	☐	☐
Pills to control diabetes			
Sleeping pills	☐	☐	☐
Stomach remedies			
Laxatives	☐	☐	☐
[illegible]			
Seizure medications	☐	☐	☐
Thyroid pills			
Any other medications	☐	☐	☐

CES-D DEPRESSION SCALE

Instructions for questions: Below is a list of the ways you might have felt or behaved. Please tell me how often you felt this way during the past week.

	During the past week:	Rarely or None of the time	Some or a little of the time	Occasionally or a moderate amount the time	Most of the all of time	Don't Know
1.	I was bothered by things that usually don't bother me.	0	1	2	3	-9
2.	I did not feel like eating: my appetite was poor.	0	1	2	3	-9
3.	I felt that I could not shake off the blues even with help from my family or friends.	0	1	2	3	-9
4.	I felt that I was just as good as other people.	0	1	2	3	-9
5.	I had trouble keeping my mind on what I was doing.	0	1	2	3	-9
6.	I felt depressed.	0	1	2	3	-9
7.	I felt that everything I did was an effort.	0	1	2	3	-9
8.	I felt hopeful about the future.	0	1	2	3	-9
9.	I thought my life had been a failure.	0	1	2	3	-9
10.	I felt fearful.	0	1	2	3	-9
11.	My sleep was restless.	0	1	2	3	-9
12.	I was happy.	0	1	2	3	-9
13.	I talked less than usual.	0	1	2	3	-9
14.	I felt lonely.	0	1	2	3	-9
15.	People were unfriendly.	0	1	2	3	-9
16.	I enjoyed life.	0	1	2	3	-9
17.	I had crying spells.	0	1	2	3	-9
18.	I felt sad.	0	1	2	3	-9
19.	I felt that people dislike me.	0	1	2	3	-9
20.	I could not get "going".	0	1	2	3	-9

WOMAC QUESTIONNAIRE: The following questions concern the amount of pain you are currently experiencing due to arthritis in your joint. For each situation please enter the amount of pain recently experienced **(circle one number on each line).**

How much pain do you have?	None	Mild	Moderate	Severe	Extreme
[redacted]	[redacted]	[redacted]	[redacted]	[redacted]	[redacted]
2. Going up or down stairs	1	2	3	4	5
[redacted]	[redacted]	[redacted]	[redacted]	[redacted]	[redacted]
4. Sitting or lying	1	2	3	4	5
[redacted]	[redacted]	[redacted]	[redacted]	[redacted]	[redacted]

The following questions concern the amount of joint stiffness (not pain) you are currently experiencing due to arthritis in your joint. Stiffness is a sensation of restriction or slowness in the ease with which you move your joints **(circle one number on each line).**

	None	Mild	Moderate	Severe	Extreme
6. How severe is your stiffness after first wakening in the morning?	1	2	3	4	5
[redacted]	[redacted]	[redacted]	[redacted]	[redacted]	[redacted]

The following questions concern your physical function. By this we mean your ability to move around and to look after yourself. For each of the following activities, please indicate the degree of difficulty you are currently experiencing due to arthritis in your joint **(circle one number on each line).**

What degree of difficulty do you have with ..?	None	Mild	Moderate	Severe	Extreme
8. descending stairs..................................	1	2	3	4	5
[redacted]	[redacted]	[redacted]	[redacted]	[redacted]	[redacted]
10. rising from sitting	1	2	3	4	5
[redacted]	[redacted]	[redacted]	[redacted]	[redacted]	[redacted]
12. bending to the floor...............................	1	2	3	4	5
[redacted]	[redacted]	[redacted]	[redacted]	[redacted]	[redacted]
14. getting in/out of car	1	2	3	4	5
[redacted]	[redacted]	[redacted]	[redacted]	[redacted]	[redacted]
16. putting on socks/stockings	1	2	3	4	5
[redacted]	[redacted]	[redacted]	[redacted]	[redacted]	[redacted]
18. taking off socks/stockings	1	2	3	4	5
[redacted]	[redacted]	[redacted]	[redacted]	[redacted]	[redacted]
20. getting in/out of bath	1	2	3	4	5
[redacted]	[redacted]	[redacted]	[redacted]	[redacted]	[redacted]
22. getting on/off toilet	1	2	3	4	5
[redacted]	[redacted]	[redacted]	[redacted]	[redacted]	[redacted]
24. light domestic duties	1	2	3	4	5